TO EVALUATE THE PRESENCE OF CARDIOVASCULAR ABNORMALITIES AND ITS ASSOCIATION WITH THE SEVERITY OF AIRWAY OBSTRUCTION IN STABLE COPD PATIENTS

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BONAFIDE CERTIFICATE

This is to certify that the dissertation "**TO EVALUATE THE PRESENCE OF CARDIOVASCULAR ABNORMALITIES AND ITS ASSOCIATION WITH THE SEVERITY OF AIRWAY OBSTRUCTION IN STABLE COPD PATIENTS**" is the Bonafide work done by **Dr. M.Saravanan** during his **MD (Tuberculosis and Respiratory Diseases)** course from July 2014 to April 2016 at Government Kilpauk Medical College, Chennai.

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DECLARATION BY THE GUIDE

This is to certify that the dissertation titled "**TO EVALUATE THE PRESENCE OF CARDIOVASCULAR ABNORMALITIES AND ITS ASSOCIATION WITH THE SEVERITY OF AIRWAY OBSTRUCTION IN STABLE COPD PATIENTS**" is the Bonafide work done by **Dr.M.Saravanan** during his MD **(Tuberculosis and Respiratory Diseases)** course from July 2014 to April 2016 at Government Kilpauk Medical College, Chennai, under my guidance.

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DECLARATION

I**, Dr. M.Saravanan** solemnly declare that the dissertation titled **"TO EVALUATE THE PRESENCE OF CARDIOVASCULAR ABNORMALITIES AND ITS ASSOCIATION WITH THE SEVERITY OF AIRWAY OBSTRUCTION IN STABLE COPD PATIENTS"** has been prepared by me. This is submitted to "**The Tamil Nadu Dr. M.G.R. Medical University, Chennai"** in partial fulfillment of the requirement for the award of MD degree examination branch XVII **Tuberculosis and Respiratory Diseases** from July 2014 to April 2016.

Place: Chennai **Dr.M.Saravanan**

Date:

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CONTENTS

TO EVALUATE THE PRESENCE OF CARDIOVASCULAR ABNORMALITIES AND ITS ASSOCIATION WITH THE SEVERITY OF AIRWAY OBSTRUCTION IN STABLE COPD PATIENTS

ABSTRACT

AIMS AND OBJECTIVES

1. To evaluate the presence of cardiovascular abnormalities in stable COPD patients
2. To correlate the cardiovascular abnormalities with severity of airway obstruction

MATERIALS and METHODS

It was an observational study done in department of pulmonary medicine, KMC/GTHTM, wherein 100 stable COPD patients, diagnosed and staged according to GOLD guidelines were evaluated by ECHO for cardiovascular abnormalities. Then the cardiovascular abnormalities were correlated with the severity of airway obstruction. Parameters assessed to find out the cardiovascular abnormalities were presence of pulmonary hypertension, TAPSE (systolic function of right ventricle) and Tei index (global function) of right ventricle ,Ejection fraction of left ventricle and presence of LVdiastolic dysfunction.

RESULTS

On evaluation of 100 COPD patients, 54 Patients had pulmonary hypertension. Frequency of pulmonary hypertension were 2(16.66%), 8(25.8%), 31(79.4%) and 13(72%) in mild, moderate, severe and very severe COPD respectively. In our study, TAPSE was within normal mean range in all patients. TEI index was abnormal in 59 patients of which 3(25%), 13(41%), 30(76%) and 13(72%) in mild, moderate, severe and very severe COPD patients respectively. LV systolic function was preserved and 27% had left ventricular diastolic dysfunction. Cardiac comorbidities increased with increase in severity of COPD.

CONCLUSION

Mortality and morbidity in COPD patients are mainly due to cardiac abnormalities rather than COPD itself, especially in moderate to severe COPD. In our study 59% had cardiac abnormalities and these patients are at a higher risk for death due to cardiac abnormalities. So, all stable COPD patients have to be subjected to routine ECHO to identify cardiac abnormalities early in the course of disease to reduce mortality due to cardiac abnormalities.

INTRODUCTION

GOLD defines "COPD, a common preventable and treatable disease, is characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases"[1]. Worldwide, COPD is a leading cause of death and disability. In 2020, it will be the 3rd leading cause of mortality and 5th in morbidity [2, 3]. The cost for caring of COPD patients continues to increase, with a significant proportion attributable to acute exacerbations [4] and comorbidities.

Globally, cigarette smoking is the most commonly encountered risk factor for COPD. Family history of COPD is a risk factor for COPD development, independent of family or personal smoking history, or childhood environmental tobacco exposure. The prevalence of COPD is approximately 20% in smokers and 4% in nonsmokers[5.] Even though not all smokers develop COPD, smokers still lose lung function (60 mL/year FEV1) in a dose-dependent manner[6]. "Second hand smoke" or "environmental tobacco smoke" exposure, outdoor pollution, and biomass smoke are the other factors associated with increased risk for COPD[7, 8, 9]. Smoke from biomass fuels used for cooking is an important risk factor of COPD in women in developing countries[10].The attributable fraction of COPD due to cigarette smoking is approximately 80% to 90%, [11] while other risk factors contribute by approximately 15%.

Genetic factors and gender also play a role. The strongest genetic risk factor that has been identified is mutation causing alpha-1-antitrypsin deficiency. The nicotinic acetylcholine receptor CHRNA3/5, HHIP, and FAM13A loci appear to be associated with susceptibility of the disease[12].The HHIP locus appears to be associated with the systemic components of COPD, frequency of COPD exacerbations, and FEV1/FVC ratio[13,14].Women report more dyspnea, similar severity of cough, but less sputum than men[15] and more frequent exacerbations [16,17] .

Comorbidities, defined as other chronic medical conditions, including coronary artery disease, diabetes mellitus, skeletal muscle weakness, cachexia, osteoporosis and muscle weakness, are common in chronic obstructive pulmonary disease (COPD) with variable prevalence[19].

Two theories have been put forth to explain the relationship between COPD and its manifestations and comorbidities. One view states "systemic ''spill-over'' of the inflammatory and reparatory events occurring in the lungs of patients with COPD, with the disease remaining at the centre of the process", whereas the other view states "pulmonary manifestations of COPD are one more form of expression of a ''systemic'' inflammatory state with multiple organ compromise" [20, 21]. The relationship between systemic effects and comorbidities of chronic obstructive pulmonary disease (COPD) is as depicted in the following picture.

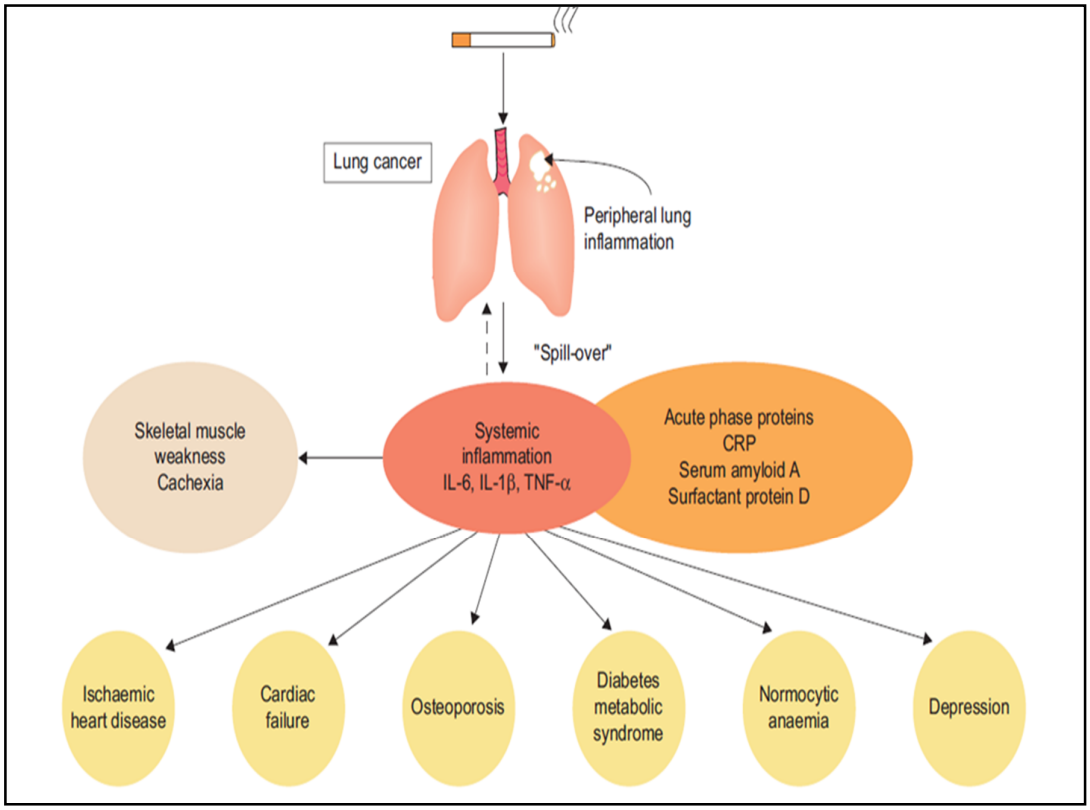


Fig 1: Systemic effects and comorbidities of chronic obstructive pulmonary disease (COPD)

Among the significant extra-pulmonary systemic comorbidities in COPD, cardiac manifestations are the most common. Up to 31% of those admitted in ICU as acute exacerbation of COPD might be due to cardiac comorbidity[24].Majority of mortality in mild or moderate COPD are due to lung cancer and cardiovascular diseases, while in more advanced COPD, respiratory failure is the predominant cause[25]. The strongest predictors of CVD are severity of airway obstruction and age. Impaired lung function itself is an independent risk factor for increased cardiovascular mortality even when adjusted for smoking status[26]. It affects pulmonary blood vessels, right ventricle as well as left ventricle leading to development of pulmonary hypertension, right ventricular dysfunction, cor-pulmonale and left ventricular dysfunction too[22, 23].

Hence assessment of cardiac condition in all COPD patients and identification of cardiac abnormalities early in the course of disease alters the mortality and morbidity in COPD significantly.

Aim and Objectives

AIM AND OBJECTIVES

1. To evaluate the cardiac abnormalities in stable COPD patients (GOLD Grades I, II, III and IV) to find out the coexisting cardiac comorbidities.

2. To correlate the cardiac abnormalities with the severity of airway obstruction.

Review of Literature

REVIEW OF LITERATURE

COPD is associated with chronic inflammatory response to noxious stimulus. Usually it is a progressive disease. Cigarette smoking is the predominant risk factor for the development of COPD. Biomass fuel used for cooking in household is the predominant cause for COPD in non-smokers especially women. In industrialised countries, air pollution and indoor pollution cause COPD. Smoking not only causes respiratory diseases but can affect many systems. CAHD, aero-digestive tract malignancy, Thrombo-angiitisobliterans etc. are associated with smoking. Lung function declines with the continuation of smoking. Various studies suggest that there is a decline of 60ml/year in the FEV1 value in smokers whereas in non-smokers it is 30ml/year [6].

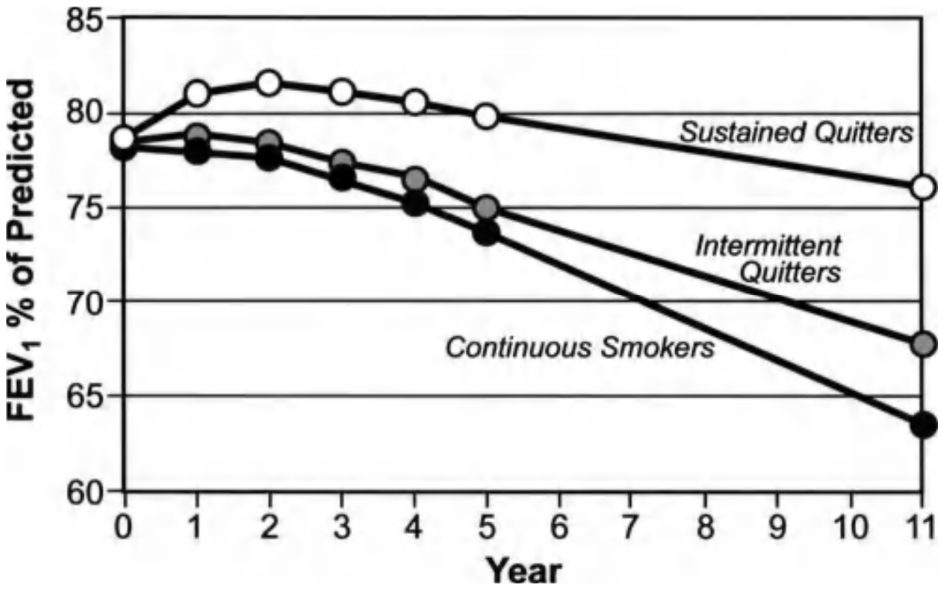


Fig. 2 - This graph depicts the continuous decline of more lung function in continuous smokers than intermittent and sustained quitters.

SMOKING INDEX

Smoking index is calculated as the product of number of cigarettes or bidis smoked per day and the duration of smoking habit in years. Thus smoking index takes into account both the quantity and the chronic nature of the problem.

The severity of smoking was measured based on Smoking Index as given in table.[56]

Severity of Smoking Index

Smoking Index	Severity of smoking
<100	Light Smokers
100 – 300	Moderate Smokers
>300	Heavy Smokers

NATURAL HISTORY OF COPD[18]

1. There is an increase in lung function with growth in childhood and adolescence.
2. Events in foetal and childhood period can affect lung growth and development which reduces the maximally attained lung function.
3. After completion of growth of lung, lung function will remain constant for some time termed as the "plateau phase", after which lung function will decline at an accelerating rate as age increases.
4. Smoking reduces this "plateau phase" duration and accelerates the rate of lung function loss.

5. Early Smoking cessation could reduce the rate of lung function loss to that of a non-smoker.

6. Patients typically present with symptoms when lung function declines below 50% of that in young adulthood.

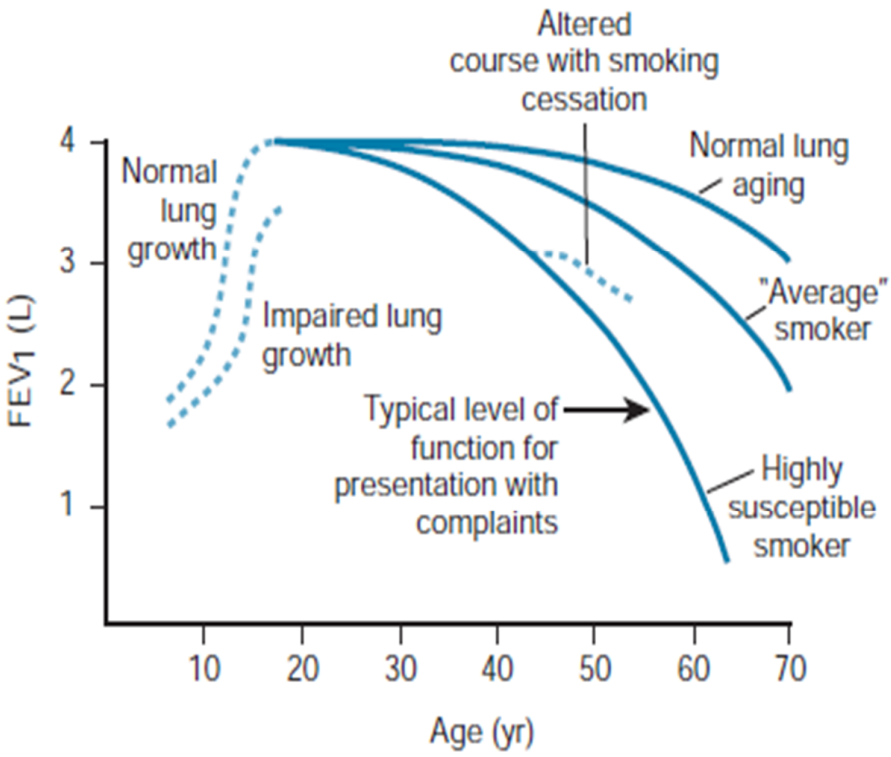


Fig 3 : Fletcher Peto curve of the natural history of COPD

Diagnosis and grading of COPD

According to the Global Initiative for Obstructive Lung Disease, airflow obstruction is considered when there is a reduction of the post bronchodilator FEV1/FVC ratio below 70% and the percentage of the post bronchodilator FEV1 of the predicted normal FEV1 is used to grade the severity of COPD.

GOLD GRADING

The following table depicts the grading of severity of COPD according to the GOLD guidelines.

Classification of Severity of Airflow Limitation in COPD (Based on Post-Bronchodilator FEV_1)		
In patients with $FEV_1/FVC < 0.70$:		
GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

Exacerbation of COPD[60]

GOLD states, "An exacerbation of COPD is an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day to- day variations and leads to a change in medication."

COPD phenotypes[60]

Clinical phenotype is defined as: "a single or combination of disease attributes that describe differences between individuals with COPD as they relate to clinically meaningful outcomes (symptoms, exacerbations, response to therapy, rate of disease progression, or death)".

Many disease characteristics (i.e., phenotypic traits) had been proposed as potential COPD phenotypes, but only a few had been validated prospectively accordingly to this definition

1. Alpha1-antitrypsin deficiency in which the specific gene/protein had been identified and specific therapy had been developed
2. Upper lobe emphysema, with poor exercise tolerance after rehabilitation, in patients with severe airflow limitation, whose survival improves with lung volume reduction surgery, and
3. Frequent exacerbations (two or more per year) that might benefit from anti-inflammatory therapy".

Following are the potential clinical COPD phenotypes that require validation. They are*

1. "Disproportionate dyspnea"
2. "Persistent systemic inflammation", -- associated with increased mortality and exacerbation rate;
3. "Chronic bronchitis",
4. Presence of chronic airway bacterial colonization
5. Emphysema and its relation with pulmonary hyperinflation and lung cancer
6. The mixed phenotype asthma/COPD and
7. "Out-of proportion" pulmonary hypertension.

COMBINED ASSESSMENT OF COPD

Symptoms

Less symptoms---- mMRC 0-1: CAT <10 patient A OR C

More symptoms – mMRC ≥2: CAT >10 patient B or D

Airflow limitation

Low risk -GOLD 1 OR 2 Patient A or B

High risk –GOLD 3 OR 4 Patient C or D

Exacerbations

Low risk - ≤1 per year and no hospitalisations per year – patient A or B

High risk - ≥ 2 per year or ≥1 hospitalisation per year- Patient C or D

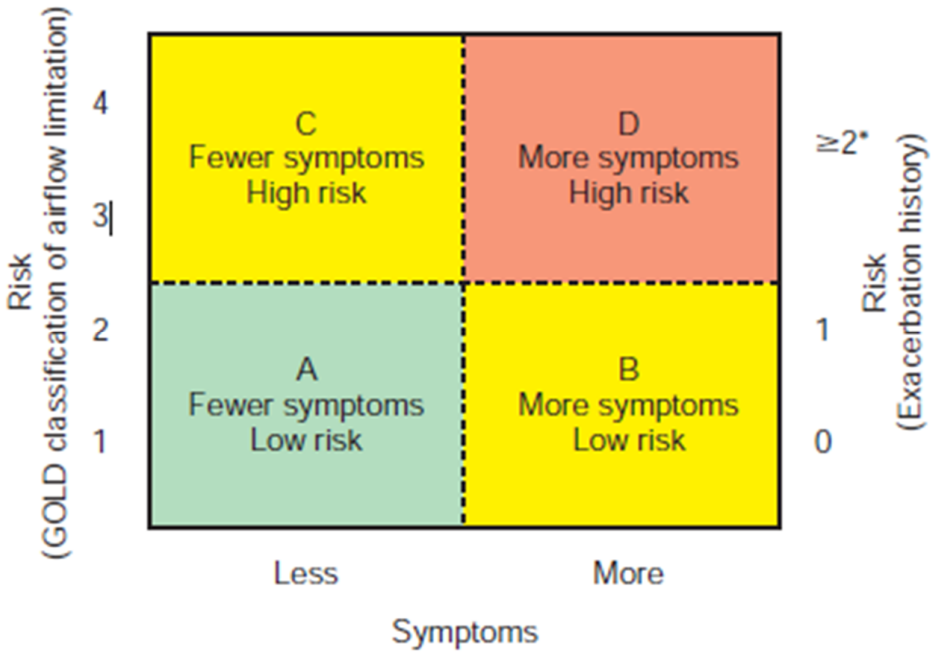


Fig. 4 : Combined Assessment of COPD

SPIROMETRY (ATS Guidelines)

Spirometry is a physiological test that measures how an individual inhales or exhales volumes of air as a function of time.

Test procedure

There are three distinct phases to the FVC manoeuvre, as follows:

1) Maximal inspiration;

2) A ‘‘blast’’ of exhalation; and

3) Continued complete exhalation to the end of test (EOT)

The patient was asked to take the deepest breath they can, and then exhale into the sensor as hard as possible, for as long as possible, preferably at least 6 seconds which was followed by a rapid inhalation (inspiration).

During the test, soft nose clips were used to prevent air escaping through the nose. Filter mouthpieces were used to prevent the spread of microorganisms.

1. Before the test, the patient's age, gender, and race are recorded
2. Height and weight are measured
3. The patient should not have eaten heavily within three hours of the test
4. He or she should be instructed to wear loose-fitting clothing over the chest and abdominal area.

Fig. 5 : Person doing spirometry

5. The respiratory therapist or other testing personnel should explain and demonstrate the breathing manoeuvres to the patient.
6. The patient should practice breathing into the mouthpiece until he or she is able to duplicate the manoeuvres successfully on two consecutive attempts.

Fig. 6 : ACCEPTABILITY CRITERIA

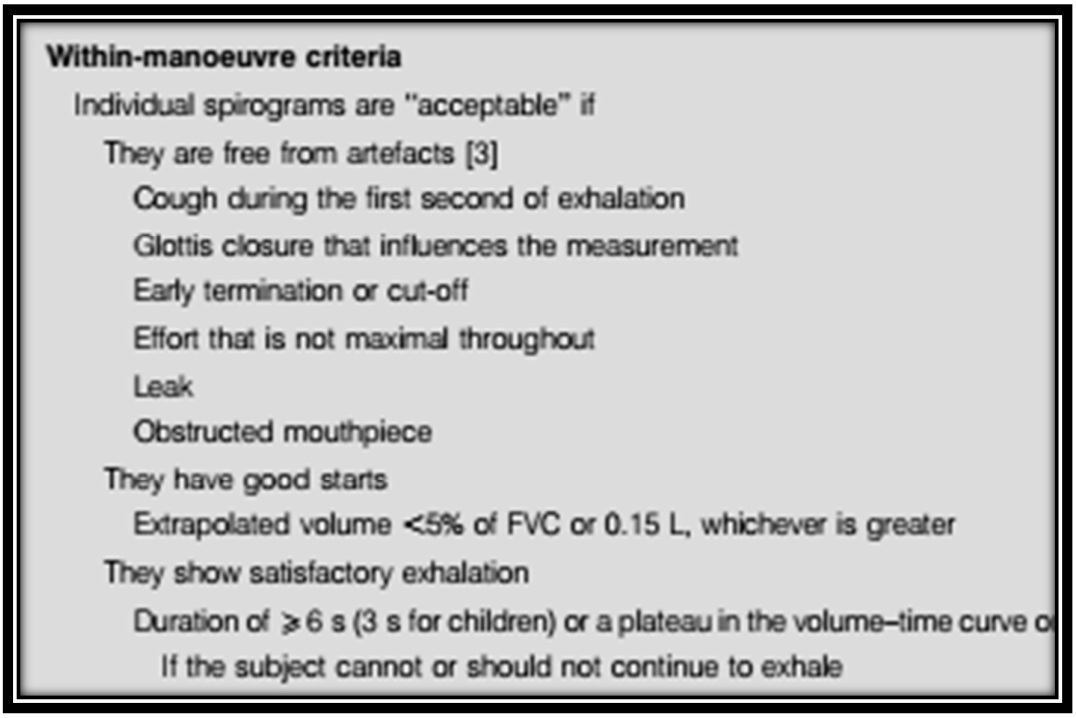
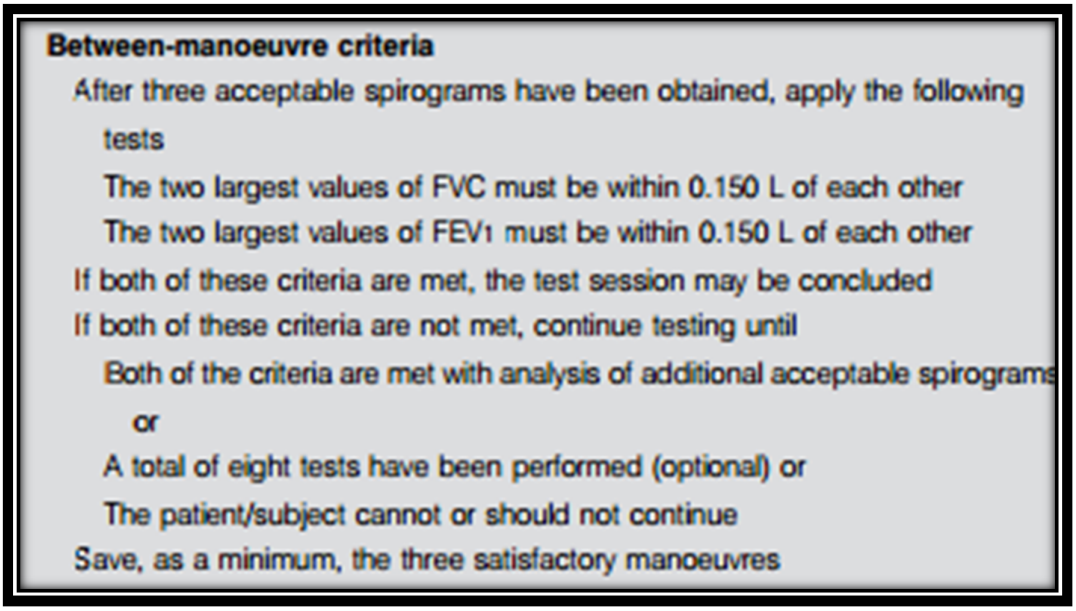


Fig. 7 : REPRODUCIBILITY CRITERIA



REVERSIBILITY TESTING

1. Stop Short-acting inhaled drugs (e.g. the βagonist albuterol/salbutamol or the anticholinergic agent ipratropium bromide) before 4 hours of testing.
2. Stop the long-acting β-agonist bronchodilators (e.g. salmeterol or formoterol) and oral therapy with aminophylline or slow release β-agonists 12 hours prior to the test.
3. Avoid smoking for >1 hour prior to testing and throughout the duration of the test procedure.
4. The subject has to do three acceptable tests of FEV1, FVC and PEF as described previously.
5. Short acting bronchodilator(salbutamol) is then administered.
6. After 10 -15 minutes of salbutamol nebulization, another three acceptable tests are recorded.

POSTBRONCHODILATOR REVERSIBILITY

The percentage improvement in FEV1 can be calculated as follows:

$$\frac{\text{(Post bronchodilator FEV1 - Prebronchodilator FEV1) X 100}}{\text{Prebronchodilator FEV1}}$$

Significant reversibility:

Increase in the post bronchodilator FEV1 more than 15 per cent of the pre-trial value or more than 200ml is considered as positive response.

CARDIOVASCULAR COMORBIDITY IN COPD

Coronary heart disease and COPD are sharing the common risk factor, i.e. smoking. Therefore it won't be surprising that there will exist a strong epidemiological link between them. When there is decrease of 10% in FEV1, cardiovascular mortality increases by 28% and non-fatal coronary events increases by 20%. [30]

Wenjia Chen et al [31] did a study named "Risk of cardiovascular comorbidity in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis". They analysed 18,176 unique references and included 29 datasets in the meta-analyses. They concluded "Compared with the non-COPD population, patients with COPD were more likely to be diagnosed with cardiovascular disease (odds ratio [OR] 2.46; 95% CI 2.02–3.00; $p<0.0001$), including a two to five times higher risk of ischaemic heart disease, cardiac dysrhythmia, heart failure, diseases of the pulmonary circulation, and diseases of the arteries. Additionally, patients with COPD reported hypertension more often (OR 1.33, 95% CI 1.13–1.56; $p=0.0007$), diabetes (1.36, 1.21–1.53; $p<0.0001$], and ever smoking (4.25, 3.23–5.60; $p<0.0001$). The associations between COPD and these cardiovascular disease types and cardiovascular disease risk factors were consistent and valid across studies. Enrolment period, age, quality of data, and COPD diagnosis partly explained the heterogeneity."

Thus COPD patients are at more risk of CVD than non-COPD necessitating a routine cardiac work-up in all COPD patients.

PULMONARY HYPERTENSION AND COPD

Barbara et al[34] reviewed the different aspects of pulmonary hypertension associated with COPD. While elucidating the natural history of pulmonary hypertension in chronic obstructive pulmonary disease, emphasised "pulmonary hypertension progresses over time and its severity correlates with the severity of airflow limitation".

Various factors contribute to the development of pulmonary hypertension in COPD. Among them, the most significant are pulmonary vasculature remodelling (shown in the picture) and pulmonary vasoconstriction in response to hypoxia.

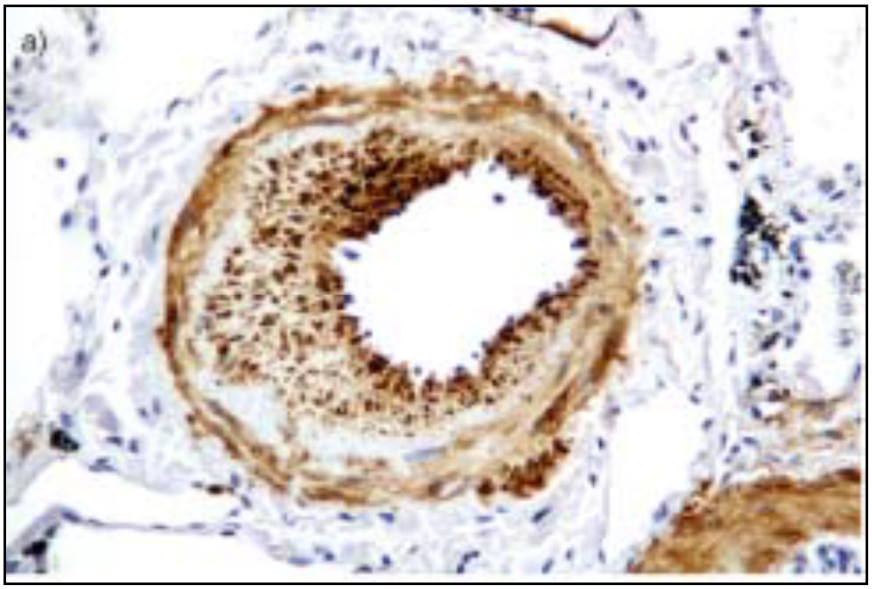


Fig. 8 : Vascular Changes

Altered endothelial function and inhibition of NO result in up-regulation of the gene expression of VEGF and increase in cellular proliferation and vessel remodelling in pulmonary hypertensive states [32,33]. Similar changes are observed both in patients with and without COPD . From this it is clear that some other factors are also contributing to the development of pulmonary hypertension in COPD. It has been postulated that inflammation and cigarette-smoke products have direct effect on vessels.

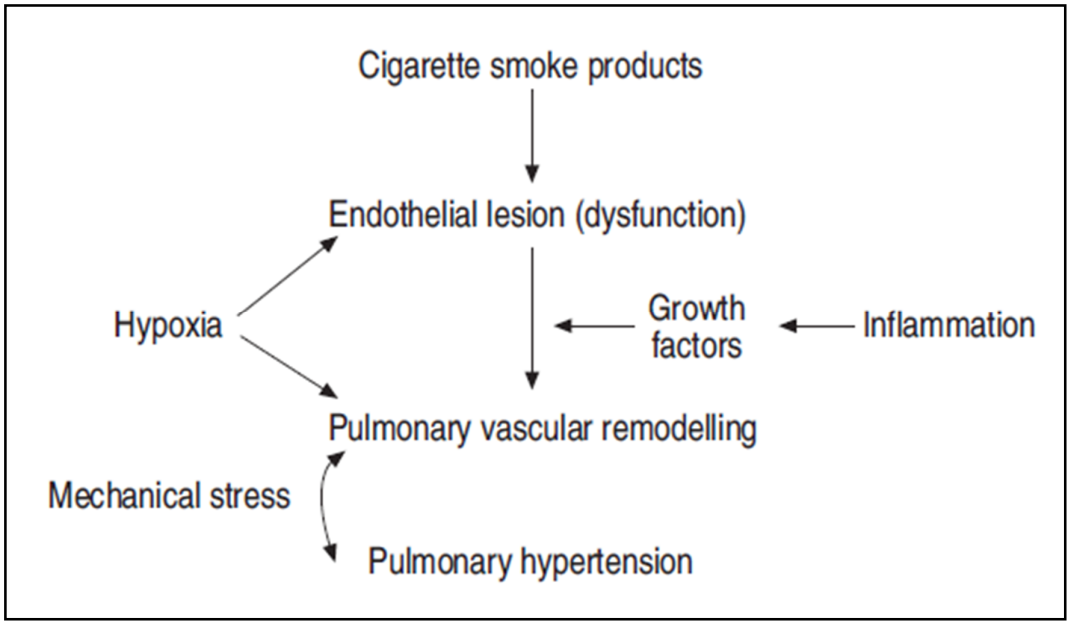
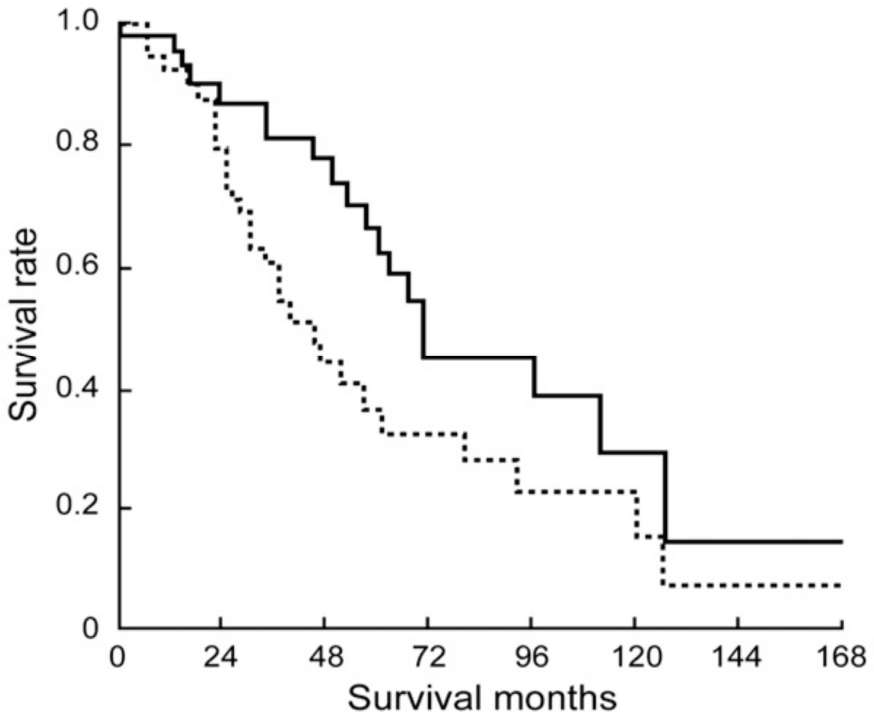


Fig 9 : Pathophysiology of pulmonary hypertension in COPD

IMPACT OF PH ON SURVIVAL OF COPD PATIENTS

The following graph depicts the impact of PH on survival in patients with advanced COPD. Oswald Mammosser et al stated" Patients with COPD with a mean pulmonary artery pressure (mPAP) of 25 mm Hg (dashed line) at the beginning of long-term oxygen therapy had a significantly (P = .001) shorter life expectancy than patients with an mPAP of < 25 mm Hg (solid line)" and also stated "Only long-term oxygen therapy has been shown to be beneficial, which stabilises PH in certain patients with COPD".[21]



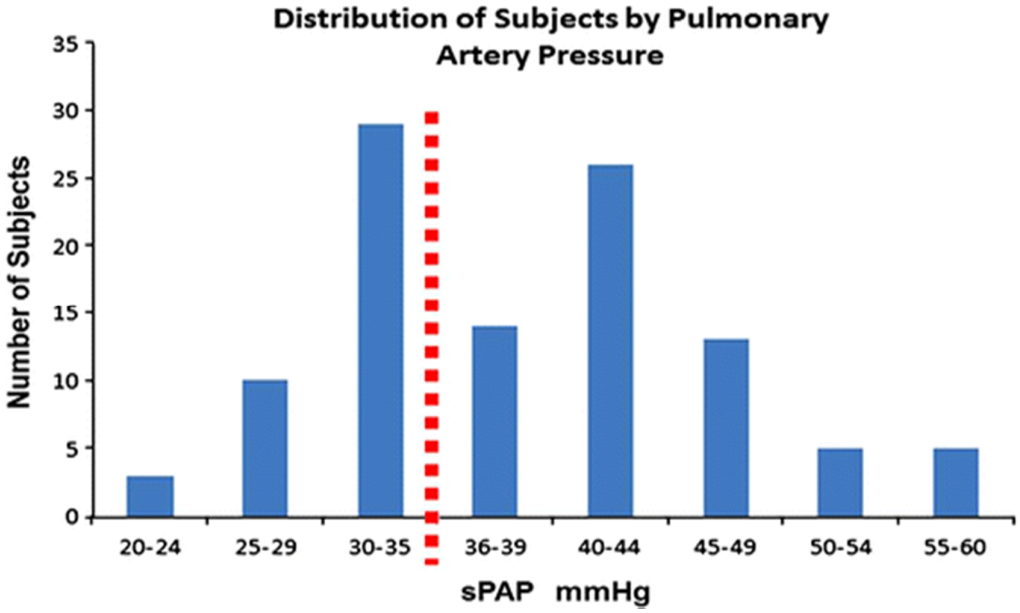
PULMONARY ARTERY CATHETERIZATION

It is considered as the gold standard in the assessment of pulmonary hemodynamics. As it is an invasive procedure, its routine use in the evaluation of COPD is precluded. However, in patients in whom significant elevations are suspected or under evaluation for potential LVRS or transplant, its use is justifiable. Pulmonary hypertension (PH) is defined as an" increased mean pulmonary artery pressure >25 mmHg at rest as assessed by right heart catheterisation (RHC)".

PULMONARY HYPERTENSION AND COPD

1. In the article "Pulmonary hypertension in chronic obstructive pulmonary disease" Barbera, Peinado, Santos concluded that most studies reported 30 -70% prevalence of PH in COPD and PH typically occurred in severe COPD patients (FEV1 value < 30% predicted) and who had hypoxemia. Severe PH (defined as mPAP > 40 mm Hg) was uncommon (1–3%) in COPD [34].

2. Vadim Fayngersh, Fotios Drakopanagiotakis, F. Dennis McCool, James R. Klinger did a study named " Pulmonary Hypertension in a Stable Community-Based COPD Population" in which they found that in 105 individuals with demonstrable TR jet, 63(60%) had PH (>36mmhg). When cut-off value for PH was increased to 40mmHg, still 49 (47%) persons had PH. They said "It was likely that some of the individuals in whom a jet could not be visualized also had PH" [35].



3. SCHARF et al [36] reported a very high incidence of PH (91%) (mPpa more than 20mmHg). There was slow rate of progression of PH in COPD and mPpa was found to be moderately elevated, even in patients with advanced disease.

4. In 1981, WEITZENBLUM et al. [37] showed in 175 patients with COPD, the incidence was 35% and also said “those with Ppa (20 mmHg) had a shorter survival than those whose Ppa was normal”.

5. Chaouat et al [38] in “Severe pulmonary hypertension and chronic obstructive pulmonary disease” with 998 severe COPD , the prevalence of severe PH (Ppa > 40 mm Hg) was 2.7%. But 50% of them had non-COPD etiologies to explain that. Thus the prevalence of severe PH is uncommon in COPD.

6. N.K. Gupta et al [39] in a study with 27/40 COPD of demonstrable TR jet in ECHO,63% had PH .The following table shows the frequencies of PH(SPAP > 30 mmHg) in various COPD grades.

Severity of COPD	% and number of patients with PH
Mild (18)	16.7% (3)
Moderate (11)	54.6% (6)
Severe (5)	60% (3)
Very severe (6)	83.3% (5)

Frequency of PH increases as the severity of COPD

Severity of COPD	% and number of patients with PH
Mild (18)	11.11% (2)
Moderate (11)	9% (1)
Severe (5)	40% (2)
Very severe (6)	33.33% (2)

NO co-relation exists between frequency of cor pulmonale and severity of COPD

7. Similarly Barbera` and Blanco [40] also found high prevalence of PH in patients with advanced COPD and said “In milder forms PH might not be present at rest but may develop during exercise”.

8. Rabab et al [41] reported in their study about LV function in patients with or without PH comprising 36 copd and 12 matched control group, a prevalence of about 55.6% (20 COPD patients) regarding pulmonary hypertension [one mild (12.5%), 5 moderate (50%), 5 severe (55.6%), and 9 very severe (100%)] with highly significant difference between mild and very severe COPD ($P < 0.01$).

LV FUNCTION AND COPD

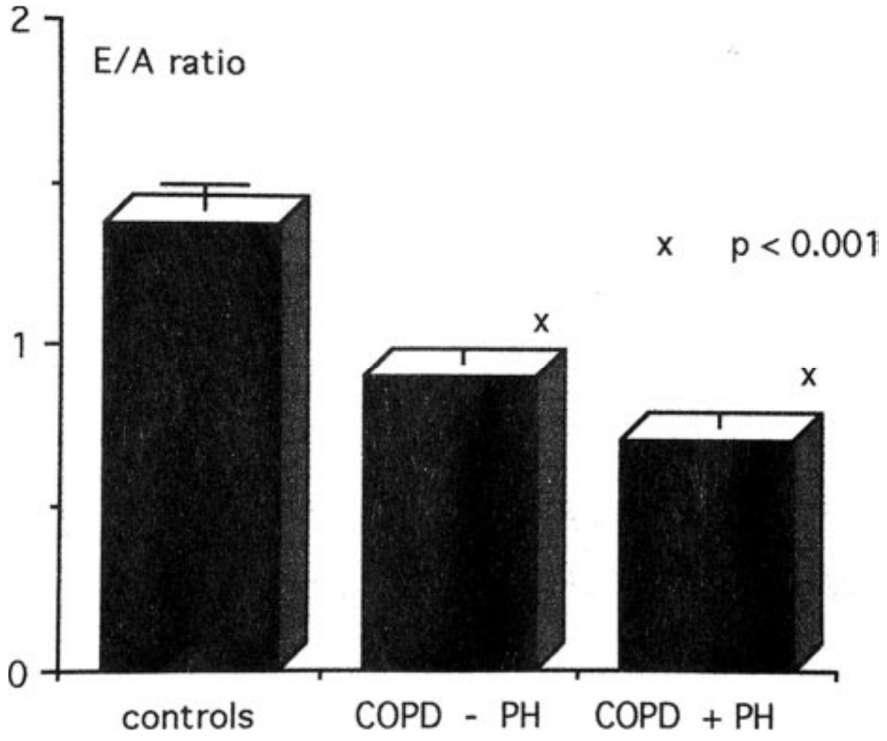
9. In the above study authors said "Left ventricular diastolic function and global function were affected in COPD patients especially with progression of the disease. COPD patients with pulmonary hypertension were more liable to LV diastolic and global dysfunction than normal pulmonary pressure COPD patients". And also concluded that Left ventricular systolic function had not shown any difference between patient and control groups [41].

10. Frans H. Rutten et al [42] found out that 50 elderly COPD patients (20.5%, 95% CI 15.6–26.1) with stable chronic obstructive pulmonary disease had unrecognized heart failure out of those 244 enrolled in the study.

11. Gupta et al [39] in their study on role of ECHO in COPD concluded that LVDD was present in (19)47.5% of patients, out of which 16 had PH and 3 did not have PH, various mechanisms might explain the presence of left ventricular diastolic dysfunction in COPD patients.

12. Lopez Sanchez et al [43] in their study on LV function in COPD reported a high prevalence of LVDD in stable severe COPD patients and concluded that "LVDD might be the reason for their lower exercise tolerance" and "Hypoxemia could have a concomitant role in their pathogenesis". In a similar study, Laura Miranda et al [44] also reported such high prevalence of LVDD in severe stable COPD patients.

13. In the study " Left Ventricular Diastolic Dysfunction in Patients with COPD in the Presence and Absence of Elevated Pulmonary Arterial Pressure", Georg-Christian Funk et al [45] reported occurrence of LVDD in COPD patients with normal PAP also.



14. Suchon´ et al. [46], found that ejection fraction, shortening fraction and lateral mitral annular peak systolic velocity (S wave) in COPD patients, were in the normal value range and did not differ significantly from control group.

15. Rabab et al [47] also concluded that LV systolic dysfunction was not found in the COPD subjects in the course of the disease.

16. Burghuber et al [48] in his study states “in the absence of conditions primarily leading to left ventricular systolic function impairment (ischemic heart disease, systemic arterial hypertension, etc.), the derangement of systolic function in the course of COPD is rarely found”.

17. A. Boussuges,et al [49],in his study stated” LVDD was present when SPAPp >60mmHg as measured by impaired relaxation type of LV dysfunction”

18. A. Moustapha, et al [50] stated “LVDD was present in 6% of copd patients with SPAP<60mmHg”.

RV FUNCTION IN COPD

Alpert JS [52], in his article on Effect of right ventricular dysfunction on left ventricular function, states “Right ventricular dilatation and hypertrophy shift the interventricular septum leftward, thereby causing decreased left ventricular cavity size, contractility, compliance, and ejection fraction as well as increased left ventricular diastolic pressure.” This phenomenon is called as “the reverse Bernheim phenomenon,”or “ventricular interaction or ventricular interdependence”.

Omar A. Minai et al [53] concluded “ Most patients with COPD-associated PH have preserved RV contractility if studied during periods of clinical

stability, 38 and studies have demonstrated RV systolic failure only among patients in the acutely decompensated state".

TAPSE

Tricuspid annular plane systolic excursion (TAPSE):**

TAPSE denotes the distance of systolic excursion of the Right Ventricle annular plane towards apex . It is measured with the M-mode cursor passing through the tricuspid lateral annulus, using 4-chamber view.It represents how much the annulus displace longitudinally at peak systole..

Views to evaluate right ventricle are shown below.

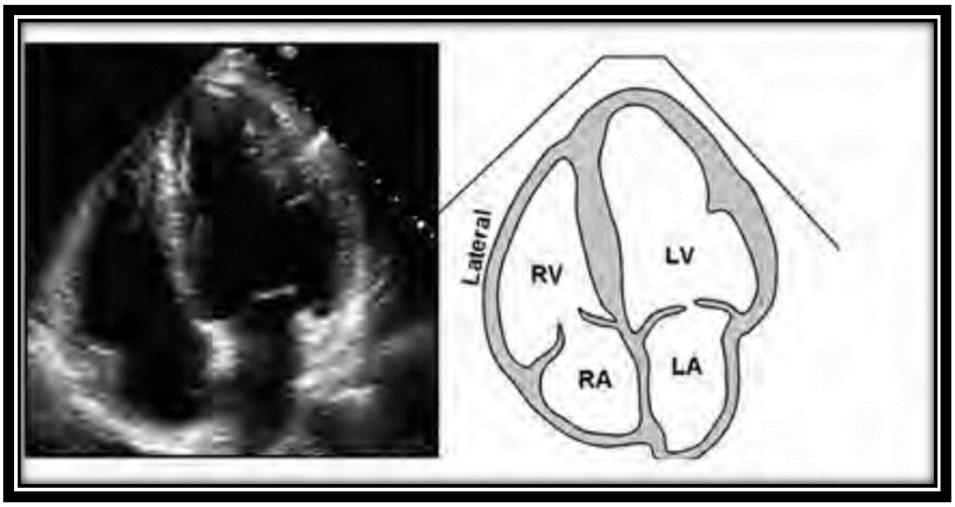


Fig. 10 : 4-chamber apical view

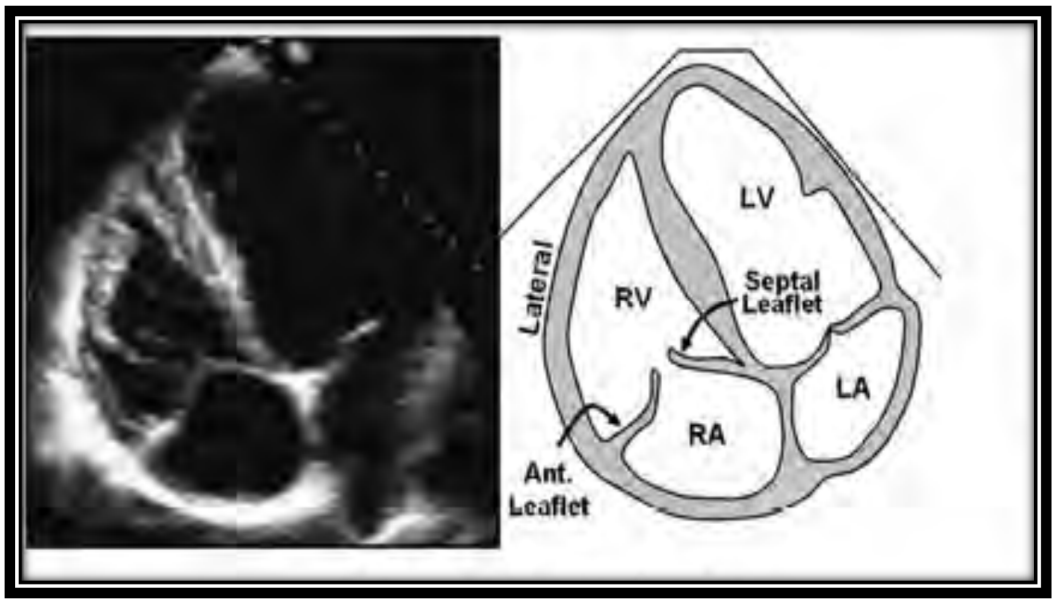


Fig. 11 : Apical – 4 – chamber view with focus on RV

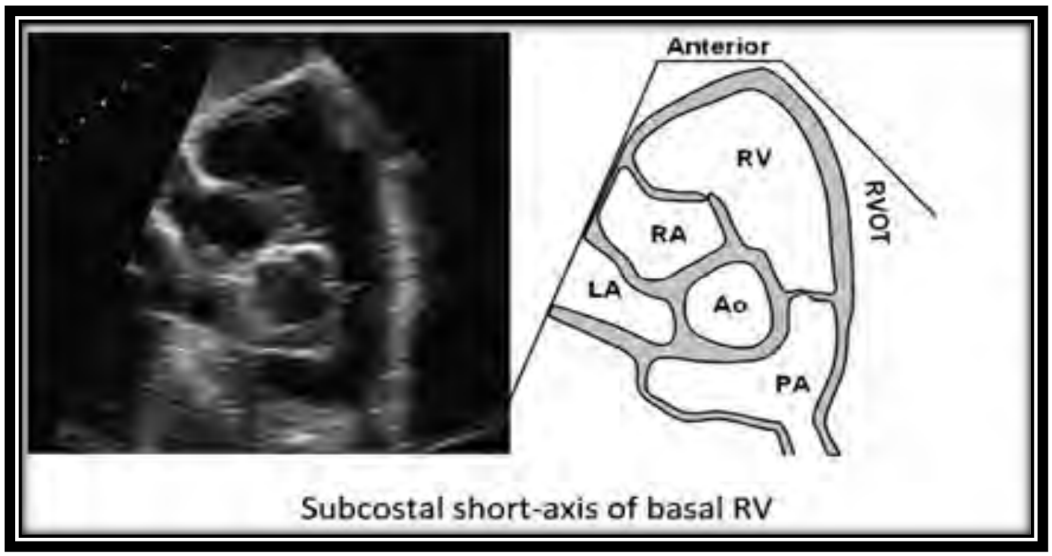


Fig. 12 : Subcostal view

TAPSE above 16 mm is considered as normal. It correlates well with various other techniques used to estimate global systolic function of right ventricle.

It is simple and relatively independent on optimal image quality and reproducible.

Disadvantages: It has been assumed that the displacement of a single segment would be represententative of the function of whole right ventricle. It depends on the angle at which it is estimated and also on the ventricular load.

TAPSE would be utilised routinely as a method of estimating RV function, keeping 16mm as cut-off value below which is considered abnormal.

TEI INDEX [54]

1. Tei index is being used to assess the global function of the right ventricle. This global myocardial performance index needs the measurements of both the tricuspid inflow and the right ventricular outflow by pulsed wave Doppler . Normal values are 0.28 ±0.04.
2. More severe the right ventricular dysfunction, more abnormal the Tei index (0.59 – 1.27 in patients with PAH)

3. Tei index is relatively less dependent on right ventricular load. It is representative of global assessment of right ventricular function independent of geometric assumptions .

It is calculated using the following formula:

$$MPI = (IVRT + IVCT)/ET$$

Where MPI = Myocardial performance index(Tei index)

IVRT = Isovolumetric relaxation time

IVCT = Isovolumetric contraction time

ET = Ejection time

There are two methods to determine Tei index :

1) The pulsed Doppler method:

For estimating Ejection Time, view adopted is parasternal short-axis view. It is done at the pulmonary valve level and based on the pulsed – wave Doppler signal at the right ventricular outflow tract.

Isovolumic intervals are derived based on the pulsed-wave Doppler envelope of the tricuspid flow. We took these measurements from two cardiac cycles. So, we must choose beats with similar R-R intervals to measure MPI accurately.

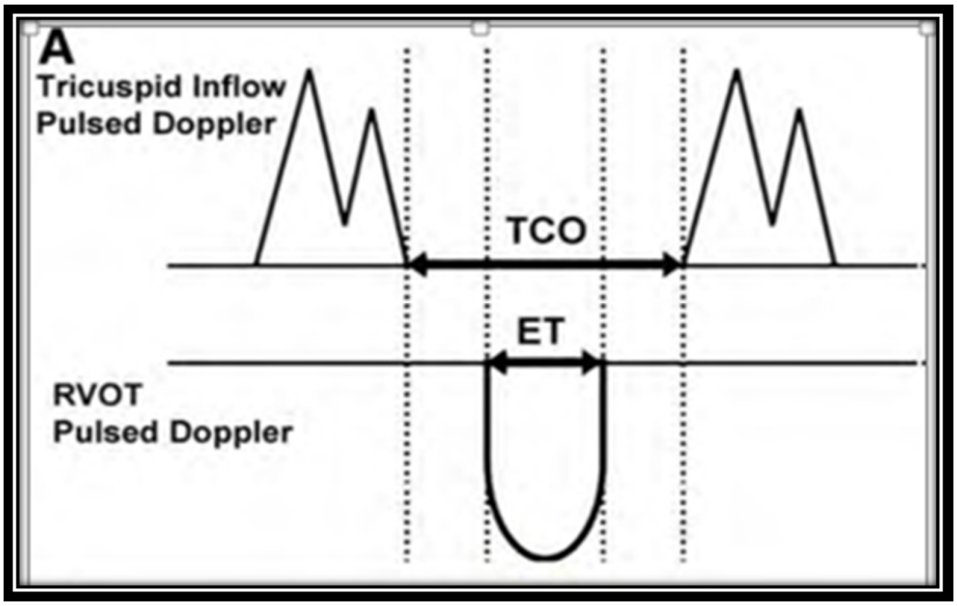


Fig. 13

The tricuspid (valve) closure opening time (TCO) encompasses isovolumic contraction time, ejection time (ET), and isovolumic relaxation time. In the pulsed Doppler method, TCO can also be measured by the duration of the tricuspid regurgitation continuous-wave Doppler signal.rom the diagram,

$$MPI = (TCO - ET)/ET$$

2) The pulsed tissue Doppler method:

In this method, based on the pulsed-wave Doppler at the tricuspid level of the right ventricular free wall, all the times such as IVRT ,IVCT AND ET are measured from a single heart-beat.

MPI would be unreliable when RA pressure was increased because of more rapid equilibration of pressures between the RV and RA, shortening the IVRT which would result in under-estimation of MPI.

Normal value of Tei index using the pulsed Doppler method is 0.28 ± 0.04.

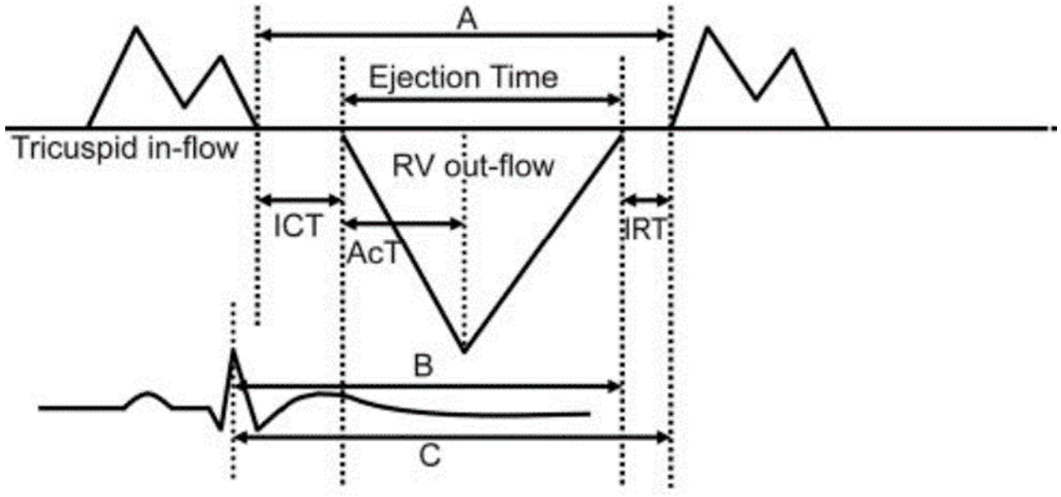


Fig. 14 : Schema of colour Doppler echocardiographic measurements

A: Interval between the cessation of tricuspid in-flow and the start of the next tricuspid in-flow.

B: Interval between the R wave and the cessation of right ventricular (RV) out-flow.

C: Interval between the R wave and the start of tricuspid in-flow.

AcT: RV out-flow acceleration time (AcT) is the interval between the start of RV out-flow and peak velocity. Ejection time (ET) is the interval of RV out-flow, measured from the start to the end of the RV out-flow Doppler velocity profile below the baseline.

Isovolumetric contraction time (ICT) = (A – ET – IRT)

Isovolumetric relaxation time (IRT) =(C – B).

The total ejection isovolume (TEI) index, which is a systolic and diastolic myocardial performance index, was calculated as (A – ET)/ET.

Systolic Pulmonary Artery Pressure (SPAP)

SPAP can be estimated using Tricuspid regurgitant velocity.

RVSP can be reliably derived from peak TR jet velocity, using the simplified Bernoulli equation and combining this value with an estimate of the RA pressure

$$RVSP = 4(V)\ 2 + RA\ pressure,$$

Where V is the peak velocity (m/s) of the TR jet.

In the absence of a gradient across the pulmonary valve or RVOT, SPAP is equal to RVSP. In cases in which RVSP is elevated, obstruction at the level of the RVOT or pulmonic valve should be excluded.

Because velocity measurements are angle-dependent, it is better to obtain TR signals from many windows and utilise high velocity signal . it will be possible in most of the patients. It is recommended that Doppler sweep speeds of 100 mm/s be used for all tracings.

1. Grading of pulmonary hypertension is as follows:[61]

Grading of PHT	SPAP
Normal	18-25mmHg
Mild	30 – 40 mmHg
Moderate	40 - 70 mmHg
Severe	>70mmHg

Doppler echocardiographic determination of systolic pulmonary artery pressure (SPAP).

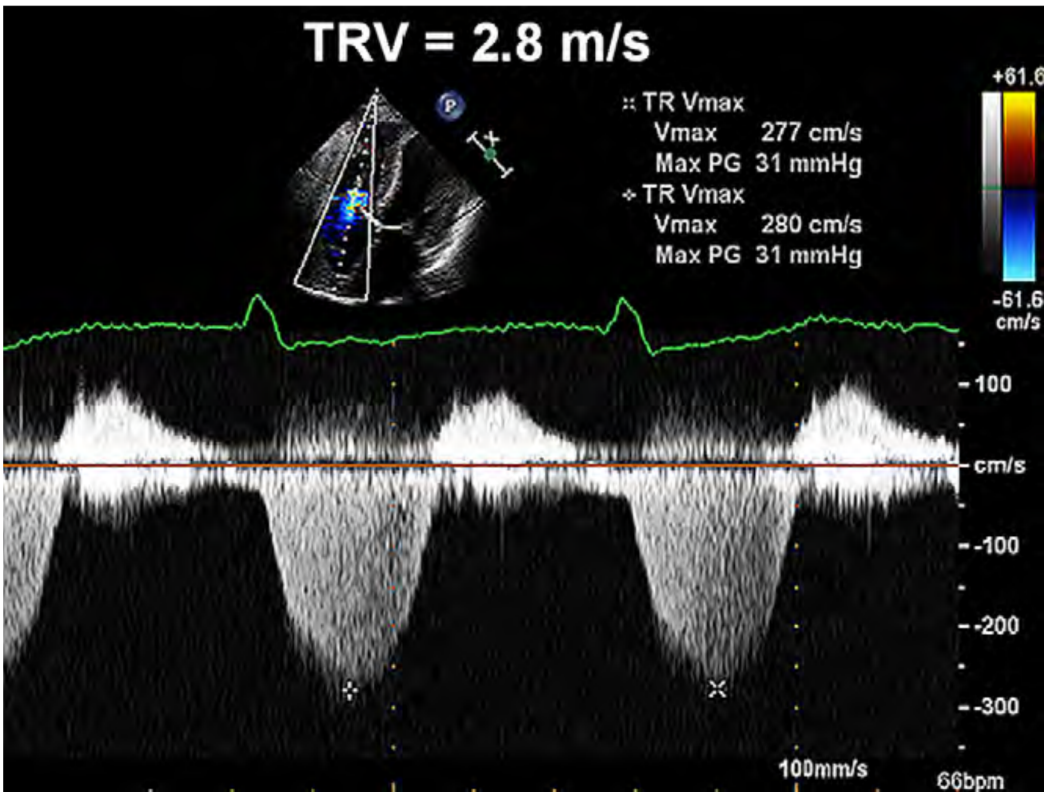


Fig.15

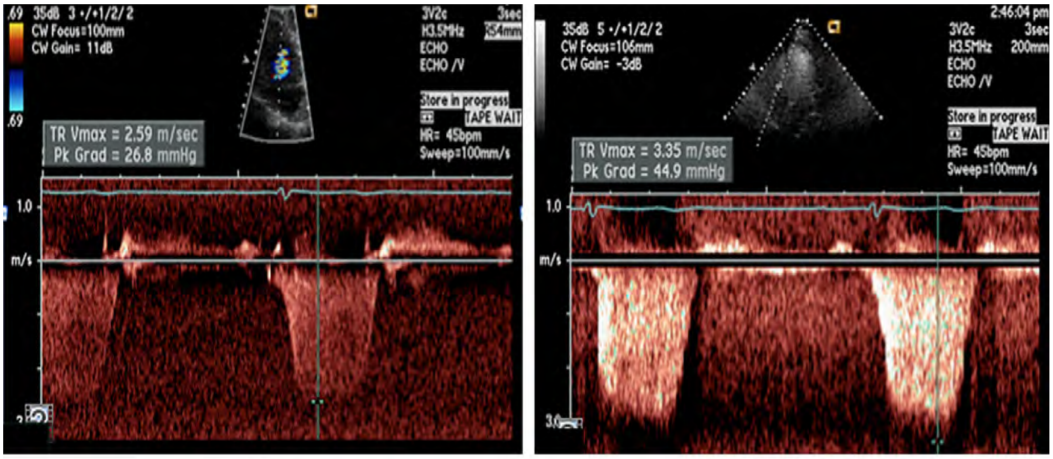


Fig.16

1. A represents Tricuspid regurgitation signal that is not contrast enhanced and correctly measured at the peak velocity.

2. B represents TR signal after contrast enhancement. Here, the clear envelope has been obscured by noise, and the reader erroneously estimated a gradient several points higher. As this example shows, it is critical that only well-defined borders be used for velocity measurement, as slight errors are magnified by the second-order relationship between velocity and derived pressure.

LV FUNCTION

1. Left ventricular function was also assessed by using :

    a. EF (ejection fraction) = measures how much volume present at the end of diastole is ejected from Left Ventricle with each systole. Normal value is above 56%.

    b. E/A = diastolic filling of left ventricles usually classified initially on the basis of the peak mitral flow velocity of the early rapid filling wave (E), peak velocity of the late filling wave caused by atrial contraction (A). In normal subjects LV elastic recoil is vigorous because of normal myocardial relaxation, therefore more filling is completed during early diastolic, so left ventricular diastolic dysfunction (LVDD) is said to be present when E/A is <1.3 (age group 45–49 years), <1.2 (age group 50–59 years), <1.0 (age group 60–69 years), and <0.8 (age group ≥70 years)[57].

ROLE OF ECHO IN EVALUATING COPD PATIENTS [54]

In the presence of tricuspid regurgitation, an estimate of systolic pulmonary artery pressure could be provided by continuous-wave Doppler echocardiography. However, tricuspid regurgitation will be present in 24–66% of COPD patients, therefore limiting the possibility to estimate SPAP in some patients. But its use is strongly recommended for the assessment of pulmonary hypertension in COPD because of the information it provides on RV function despite limitations.

With echocardiography, cases of under- and over-estimations are not uncommon.it is not possible to measure mean pulmonary artery pressure directly using this method. Therefore, echocardiography can be considered as a tool for assessing the likelihood of PH. Transthoracic echocardiography can be useful for non-invasive screening of COPD patients at risk of PH. Patients showing signs suggestive of PH in echocardiography can be referred for a confirmatory RHC.

Methodology

METHODOLOGY

Subject selection

The present study approved by the institutional ethical committee was conducted in the department of pulmonary medicine,Kilpauk Medical College, Chennai over a period of 6 months from February 2015 to July 2015.

Collaborating department : Department of Cardiology,Kilpauk Medical College,Chennai.

Patients attending the pulmonary medicine out-patient department in Kilpauk Medical College Hospital (KMCH) and Govt.Thiruvotteeswarar Hospital of Thoracic Medicine (GTHTM) with symptoms suggestive of Chronic Obstructive Pulmonary Disease (COPD) were selected.

Informed written consent was obtained from all the patients prior to inclusion in the study

A patient was suspected to have COPD if he or she was above 40 years of age and had any one of the following as advocated by Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, 201331.

1. Dyspnoea
    - o Progressive
    - o Characteristically worse with exercise
    - o Persistent

2. Chronic cough
    - o May be intermittent
    - o May be unproductive
3. Chronic sputum production
    - o Any pattern
4. History of exposure to risk factors
    - o Tobacco smoke
    - o Smoke from home cooking and heating fuels
    - o Occupational dusts and chemicals
5. Family history of COPD

INCLUSION CRITERIA

1. Smokers
2. Age above 40 years
3. Newly diagnosed or Known COPD
4. Clinically stable COPD(those who do not require change in regular medications for atleast 6 weeks)[43]
5. Second hand smoke and Biomass fuel exposure

EXCLUSION CRITERIA

1. Age less than 40 years
2. Pre-existing other respiratory diseases like active pulmonary tuberculosis, pulmonary tuberculosis sequalae, bronchiectasis, bronchial asthma, and lung malignancy.
3. Known cardiac patient (valvular heart disease, IHD) or hypertensive
4. COPD patients in acute exacerbation or history of acute exacerbation of COPD within the last two months
5. Those who are not willing for echo
6. Those who are not able to perform Spirometry.

Among the patients attending pulmonology OPD, those who had been suspected of having COPD and satisfied the inclusion and exclusion criteria were subjected first to sputum AFB smear and chest x-ray to rule out active PTB.

Then spirometry was done as per the ATS guidelines. A post-bronchodilator forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) less than 0.7 confirms the presence of airflow limitation. They were then subjected to haemoglobin, total count, differential count, ESR, blood sugar, urea and serum creatinine, cholesterol and ECG. Spirometry was done using Easyware 2 which is a computerised portable spirometer SN02134, 7.1 version.

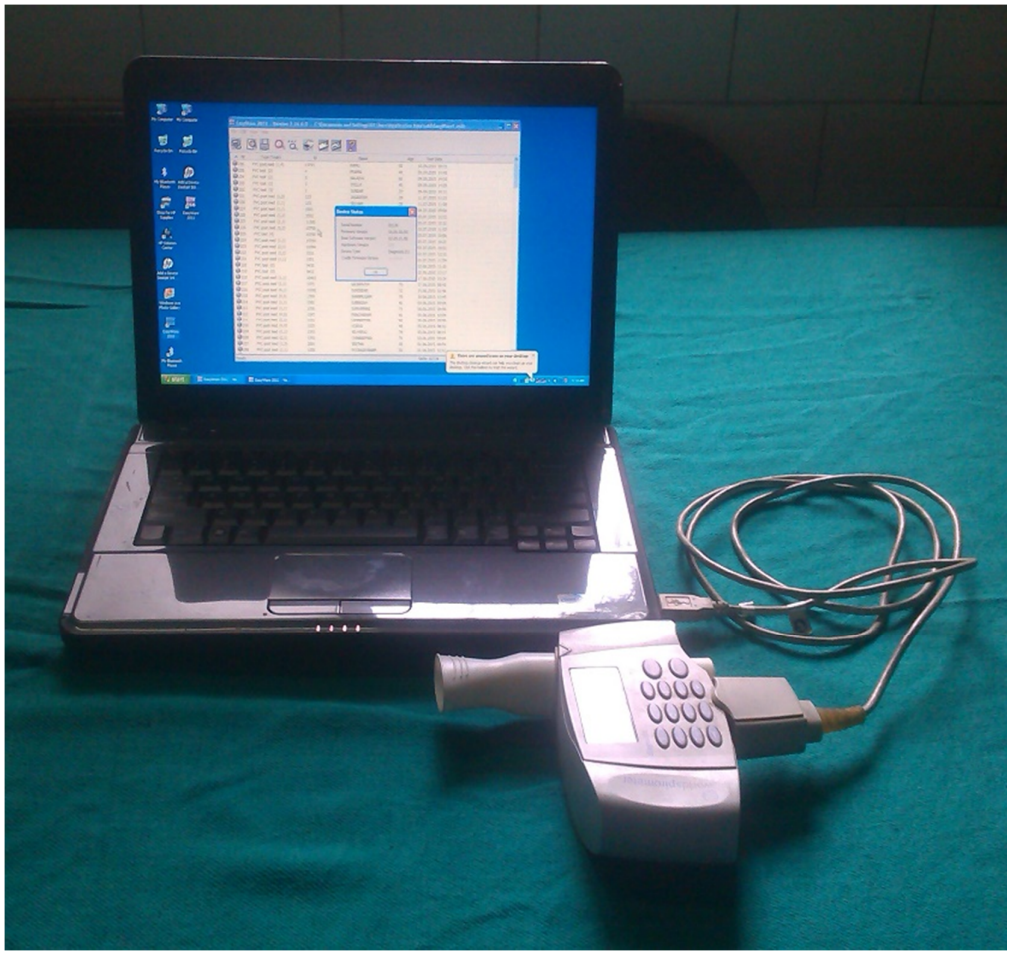


Fig.17 : Computerised spirometer - EASYWARE 2

Grading of severity of COPD was done according to GOLD guidelines.

GOLD Classification of Severity of Airflow Limitation in COPD, Based on Post-Bronchodilator FEV1**

In Patients with FEV1/FVC < 0.70

GOLD 1	Mild	FEV1 ≥ 80% predicted
GOLD 2	Moderate	50% ≤ FEV1 < 80% predicted
GOLD 3	Severe	30% ≤ FEV1 < 50% predicted
GOLD 4	Very Severe	FEV1 < 30% predicted

All patients who had been enrolled in our study were subjected to resting two-dimension transthoracic Doppler echocardiography in the cardiology department of Kilpauk Medical College and hospital by expert cardiologists. The machine used was MyLabView ECHO machine system with a multifrequency probe with a range of 2–4.3 MHz.Both 2D and M-Mode studies were done. Views adopted were apical 4-chamber view, subcostal view and RV focussed apical 4-chamber view.

Fig.18 : ESOATE My Lab FIVE ECHO MACHINE

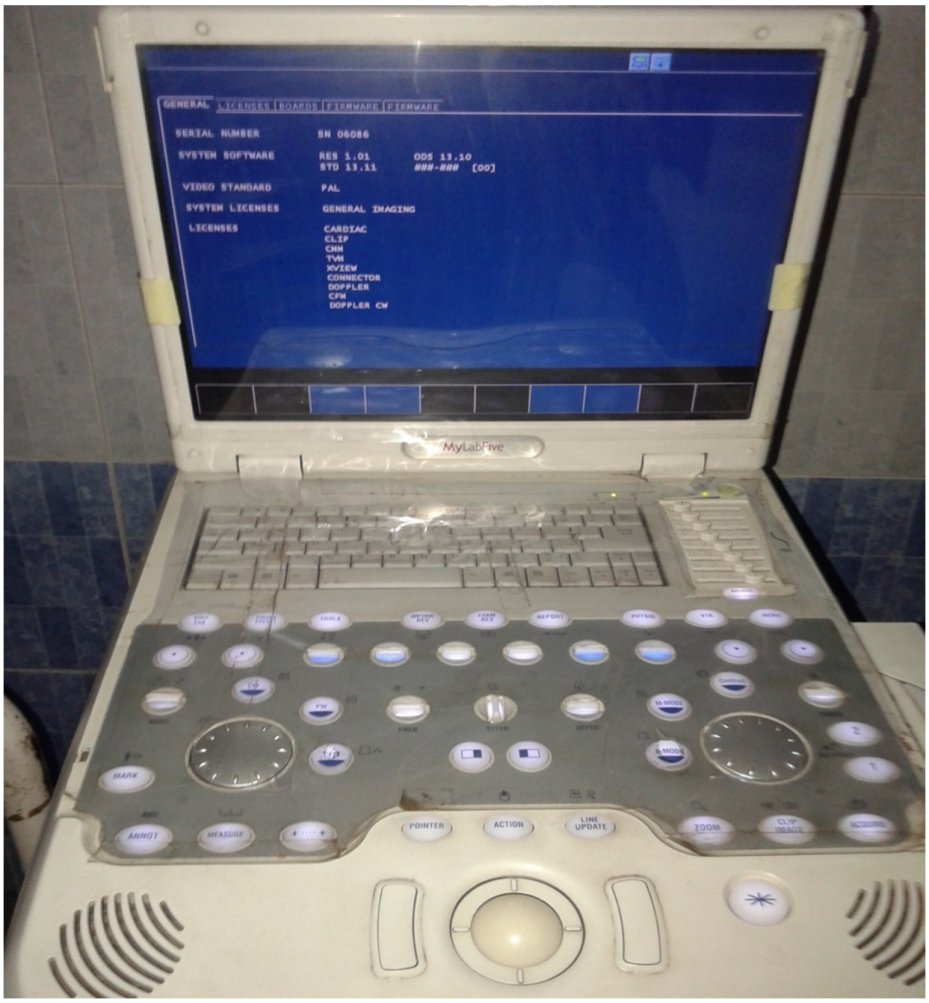


Fig 19 : ESOATE My Lab FIVE ECHO MACHINE

Assessment of the pericardium, valves and function, left atrial, left ventricular, right atrial and right ventricular size and cardiac function was done. Tricuspid regurgitant flow had been identified by colour flow Doppler technique. By continuous wave Doppler without the use of intravenous contrast, maximal Tricuspid regurgitant flow was observed…

We estimated the Right ventricular systolic pressure as per the modified Bernoulli equation. It had been considered to be equal to the SPAP (systolic pulmonary artery pressure) when there was absence of right ventricular outflow obstruction.

SPAP (mmHg) = RVSP = TTPG +RAP

Where RVSP = right ventricular systolic pressure,

TTPG = trans-tricuspid pressure gradient and

RAP = right atrial pressure (RAP),

Where trans-tricuspid gradient is 4v2 (v = peak velocity of tricuspid regurgitation, m/s).

We had taken a fixed value of 10 mmHg as right atrial pressure.

Pulmonary hypertension (PH) was said to be present when SPAP $\geq$ 30 mmHg. This value was chosen according to the definition of pulmonary hypertension. PH was classified into mild, moderate, and severe category as SPAP 30–40, 40–60, >60 mmHg, respectively.

Right ventricular systolic function was assessed by TAPSE (Tricuspid Annular Plane Systolic Excursion) and its global function was assessed by Tei index.

TAPSE was considered abnormal when it was less than 16mm

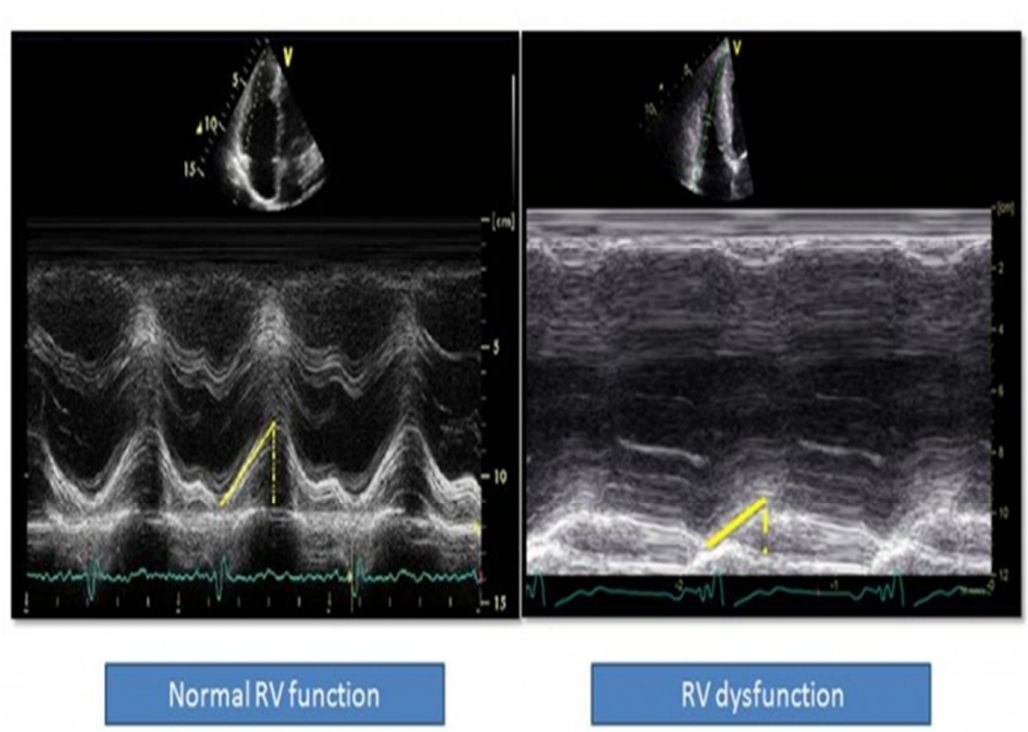
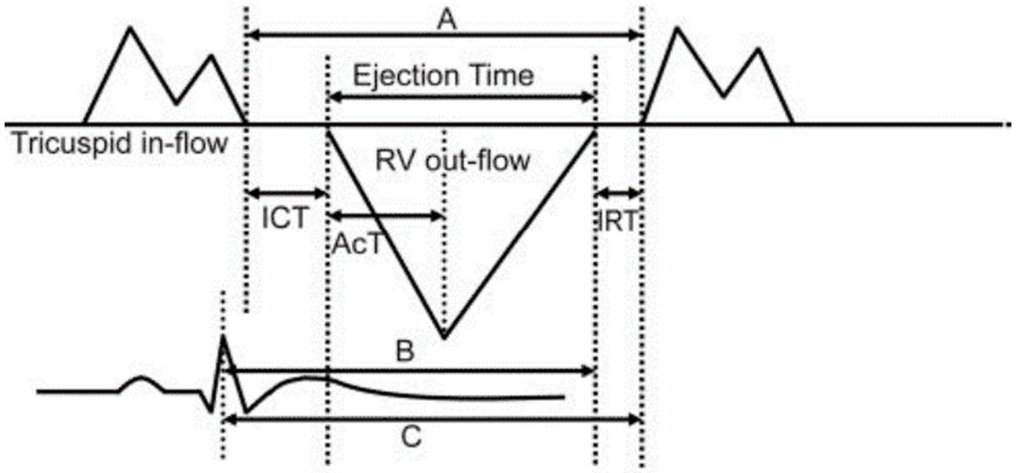


Fig. 20

Tei index was calculated using the following formula:

- MPI = (IVRT + IVCT)/ET



Isovolumetric contraction time (IVCT) = (A – ET – IRT)

Isovolumetric relaxation time (IVRT) =(C – B).

The total ejection isovolume (TEI) index, which is a systolic and diastolic myocardial performance index, was calculated as (A – ET)/ET.

Normal mean range of Tei index is 0.28+/-0.04

We assessed the Left ventricular function by using the following parameters:

EF (ejection fraction) = measure of how much end-diastolic value is ejected from LV with each contraction (56%–78%).

E/A = diastolic filling of left ventricles usually classified initially on the basis of the peak mitral flow velocity of the early rapid filling wave (E), peak velocity of the late filling wave caused by atrial contraction (A). In normal subjects LV elastic recoil is vigorous because of normal myocardial relaxation, therefore more filling is completed during early diastolic, so left ventricular diastolic dysfunction (LVDD) is said to be present when

E/A is <1.3 (age group 45–49 years),
<1.2 (age group 50–59 years),
<1.0 (age group 60–69 years), and
<0.8 (age group ≥70 years). [13]

Study Design	:	Cross-Sectional Observational Study
Place of Study	:	Kilpauk Medical College and GTHTM, Otteri.
Duration of Study	:	6 months(from Feb 2015 to July 2015)
Sample Size	:	100
Sampling	:	Consecutive COPD patients attending OPD

All data collected were analysed by SPSS version-17 for mean, SD, chi-square test and Pearson Correlation Test.

Results

RESULTS

PATIENT CHARACTERISTICS

1.GENDER DISTRIBUTION

A total of 100 COPD patients who fulfilled the inclusion criteria were included in the study after obtaining informed consent. Of the 100 patients, 89 were males and 11 were females. Thus males accounted for 89% of our study population while females accounted for 11%.

Table 1 : Gender Distribution

GENDER	NO. OF PATIENTS
MALE	89
FEMALE	11
TOTAL	100

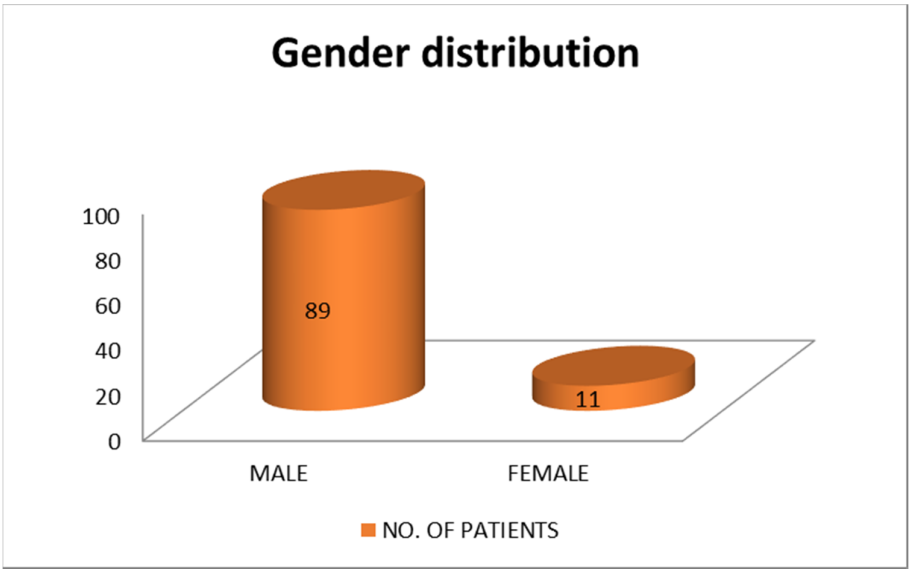


Fig 21 : Gender distribution

2.AGE DISTRIBUTION

Age group of our study population was in the range of 42 to 86 years. The mean age of the study population was 59.31 with the standard deviation of 9.230. The number of patients in the age group 40-50,51-60,61-70,71-80,and >80 years were 21(21%),32(32%),42(42%) ,3 (3%) and 2 (2%) respectively.

Table 2 : Age Distribution

AGE (years)	MALE	FEMALE	TOTAL
40-50	17	4	21
50-60	27	5	32
60-70	40	2	42
70-80	3	0	3
>80	2	0	2
TOTAL	89	11	100

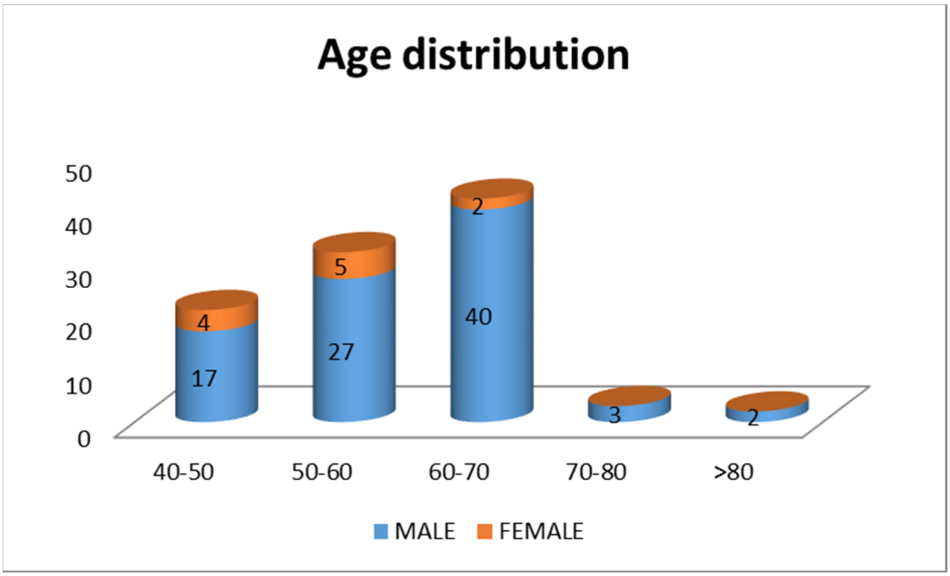


Fig.22 : Age distribution

3.SMOKING STATUS

All the 11 females in our study population were non-smokers. Among the 89 males, 18 were light smokers, 47 were moderate smokers, and 24 were heavy smokers. The smoking index of our study population ranged from 0 to 700 with a mean value of 226.08.

Table 3 : Smoking Index

GENDER	NON SMOKER	<100	100-300	>300	TOTAL
MALE	0	18	47	24	89
FEMALE	11	0	0	0	11

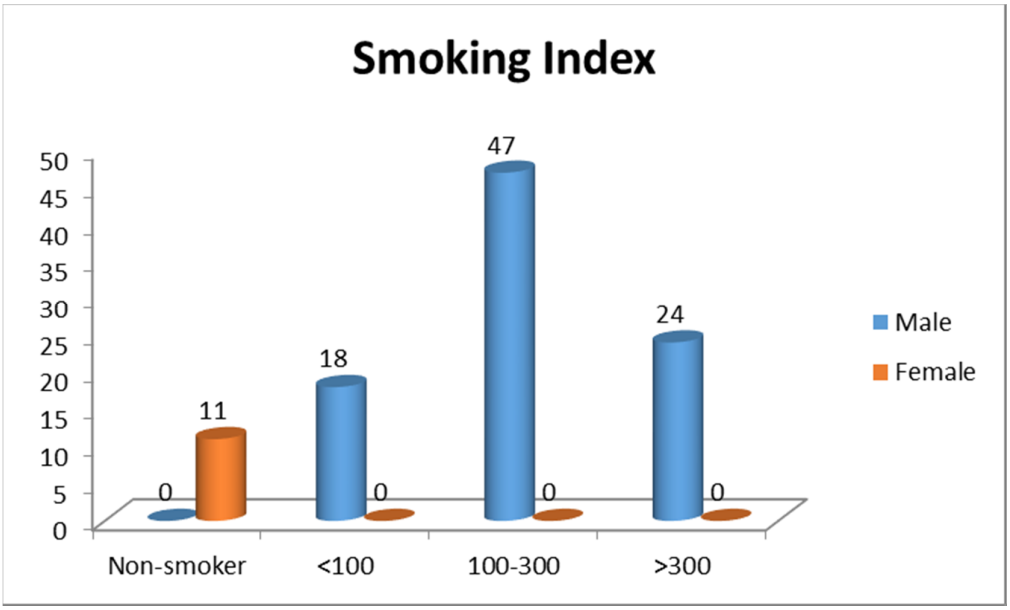


Fig 23 : Smoking status of study population

4.SMOKING STATUS AND GOLD COPD GRADE

Among GOLD 1 COPD patients, majority are light smokers 66.6%

In GOLD 2 COPD patients ,majority are moderate smokers 64.52%

In GOLD 3COPD majority are moderate smokers 53.85%

In GOLD 4 COPD, majority are heavy smokers(61.11%).

Table 4 : Smoking severity and GOLD-COPD Grade

SEVERITY OF SMOKING	COPD-GOLD GRADING				
	GOLD 1	GOLD 2	GOLD 3	GOLD 4	TOTAL
HEAVY	0	3	10	11	24
MODERATE	4	20	21	2	47
MILD	8	8	1	1	18
NON SMOKER	0	0	7	4	11
TOTAL	12	31	39	18	100

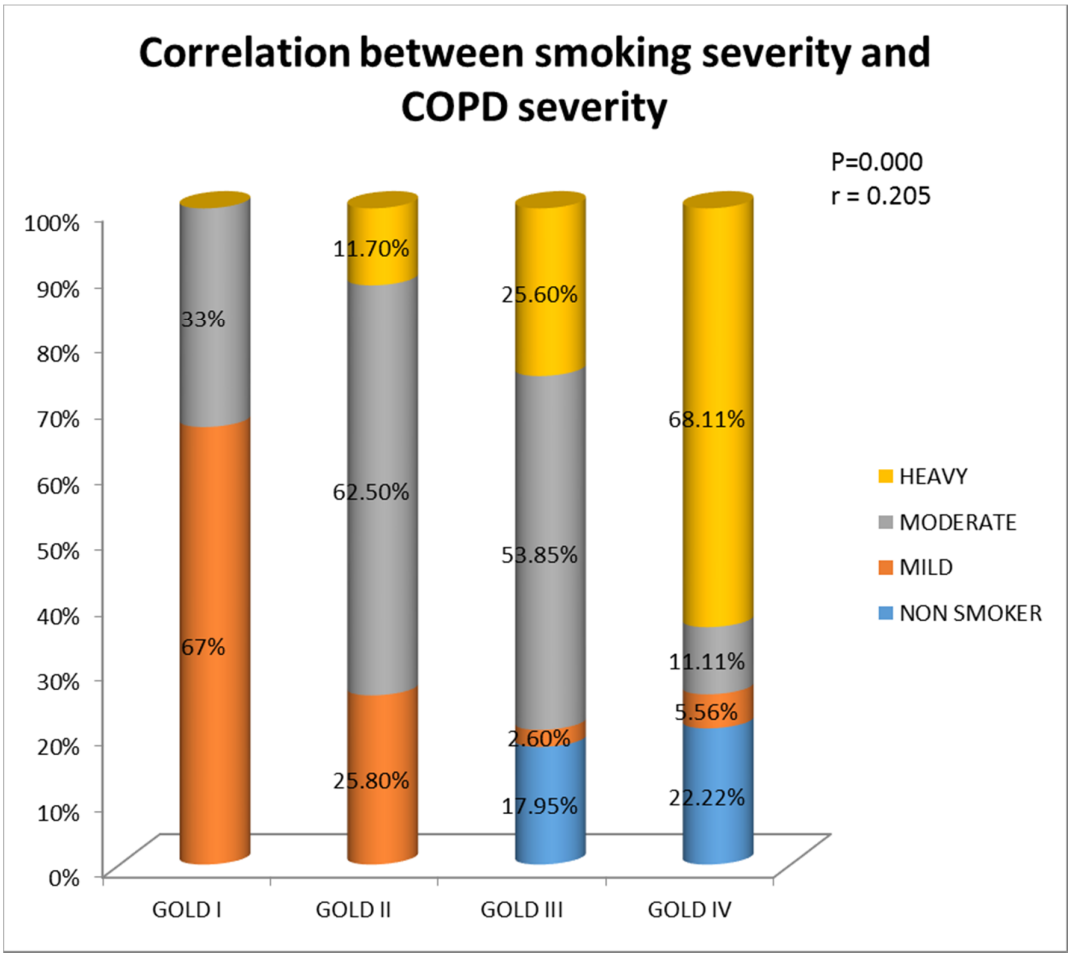


Fig.24 : Smoking severity and GOLD-COPD Grade

5.DEGREE OF AIRFLOW LIMITATION

Among females 7(7%) and 4(4%) had severe and very severe COPD and none were in mild or moderate COPD whereas among males, the number of mild, moderate, severe and very severe COPD were 12 (12%), 31(31%), 32(32%) and 14(14%) respectively. The mean FEV1% of the study population was 48.17%

Table 5 : Degree of Airflow Limitation

GENDER	GOLD1	GOLD II	GOLD III	GOLD IV	TOTAL
FEMALE			7	4	11
MALE	12	31	32	14	89
TOTAL	12	31	39	18	100

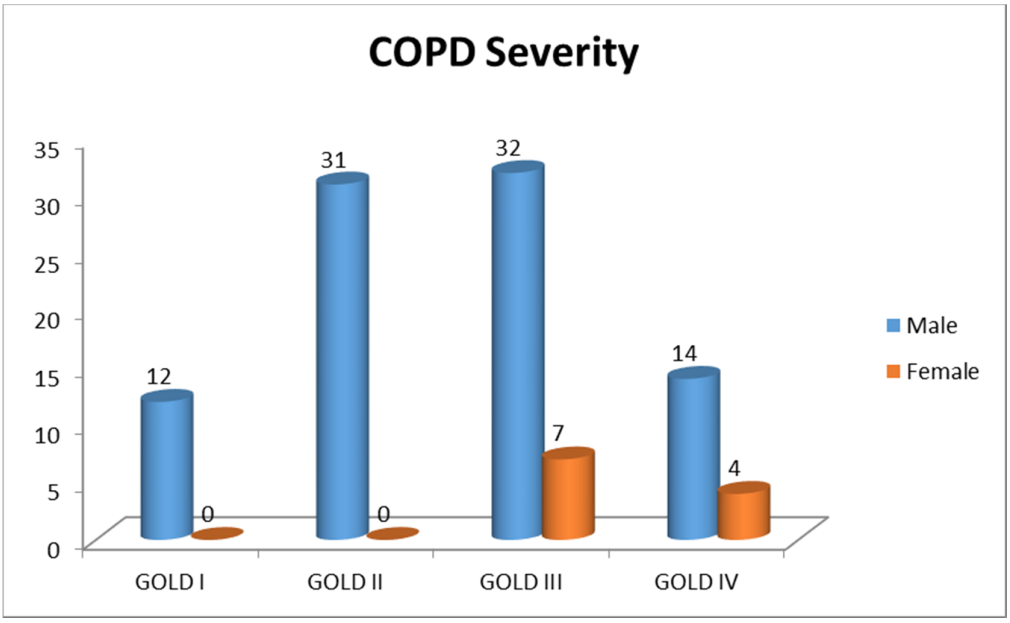


Fig.25 : COPD severity

6.AGE-WISE DISTRIBUTION OF GRADES OF COPD

Among the 21 patients of 40-50 years age group, the number of mild, moderate, severe and very severe COPD were 10(47.61%),2(9.52%),6(28.57%) and 3(14.28%) respectively.in the 32 patients of 51-60years age group, the number of mild, moderate, severe and very severe COPD were 1(3.125%),14(43.75%),11(34.375%)and 6(18.75%) respectively. among the 42 patients in the 61-70 year age group the number of mild, moderate, severe and very severe COPD were 1(2.38%), 14(33.33%), 19(45.23%) and 8(19.04%) respectively. Among 71-80 year age group, 33.33% each had moderate, severe, and very severe COPD. 2 patients with age above 80 years had severe COPD.

Table 6 : Age-Wise Distribution of Grades of COPD

AGE GROUP	GOLD I	GOLD II	GOLD III	GOLD IV	TOTAL
40-50	10	2	6	3	21
51-60	1	14	11	6	32
61-70	1	14	19	8	42
71-80		1	1	1	3
>80			2		2
	12	31	39	18	100

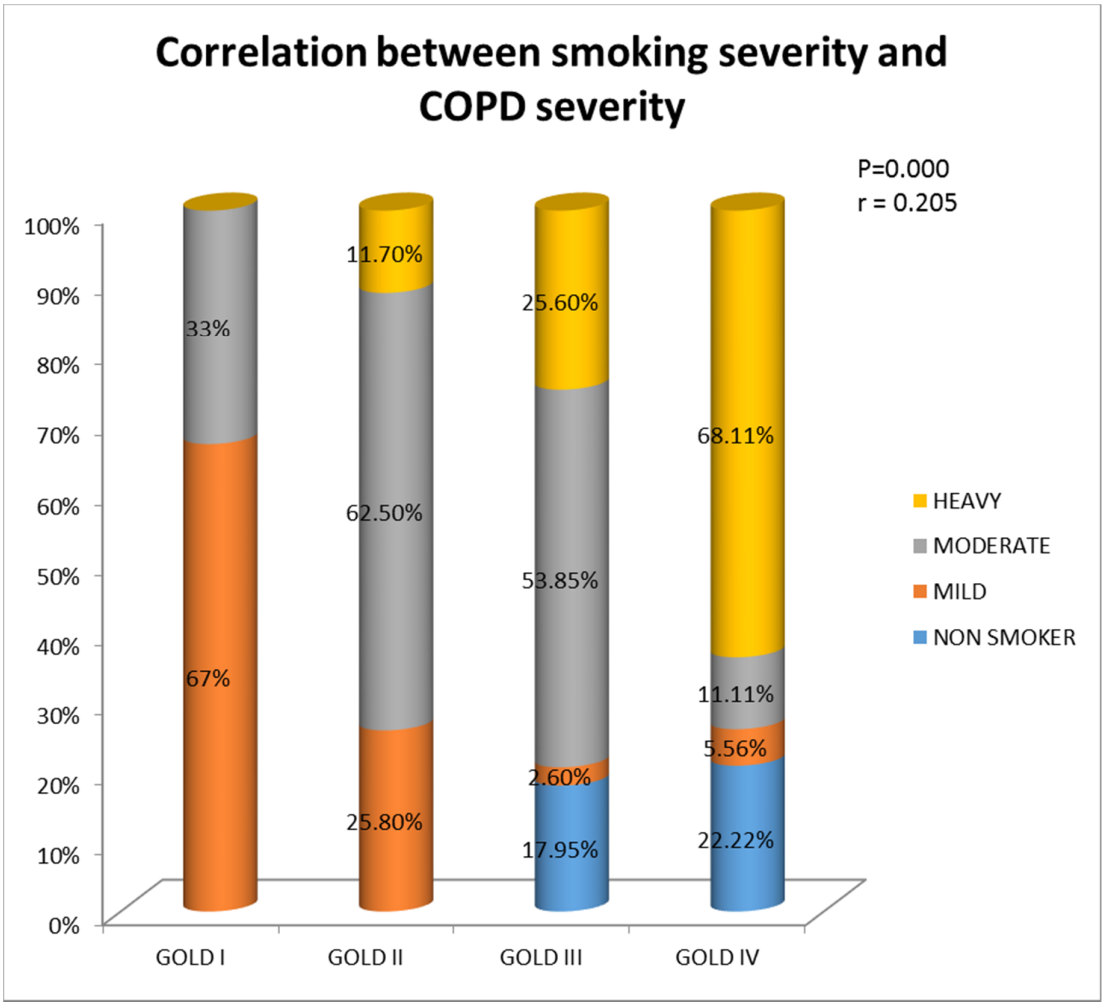


Fig. 26 : Smoking severity and COPD severity

7.COPD-GOLD GRADE AND PULMONARY HYPERTENSION

Out of the 100 patients, 54(54%) had Pulmonary hypertension of which 35(64.81%) had mild and 19 (35.18%) had moderate pulmonary hypertension. No one had severe pulmonary hypertension.

Among the 12 patients of GOLD I, 2 (16.66%) had PHT (mild PHT). Among the total 31 GOLD II patients, 8 (25.80%) had PHT (mild PHT). Among the total 39 GOLD III, 31(79.48%) had PHT of which 19 (61.29%) were of mild PHT and 12 (38.70%) were of moderate PHT.

Out of the 18 GOLD IV, 13 (72.22%) had PHT of which 6(46.15%) were of mild PHT and 7(53.84%) were of moderate PHT.

Table 7 : COPD-Gold Grade and Pulmonary Hypertension

GOLD-COPD GRADE	SEVERITY OF PHT			
	NORMAL	MILD	MODERATE	TOTAL
I	10	2	0	12
II	23	8	0	31
III	8	19	12	39
IV	5	6	7	18
TOTAL	46	35	19	100

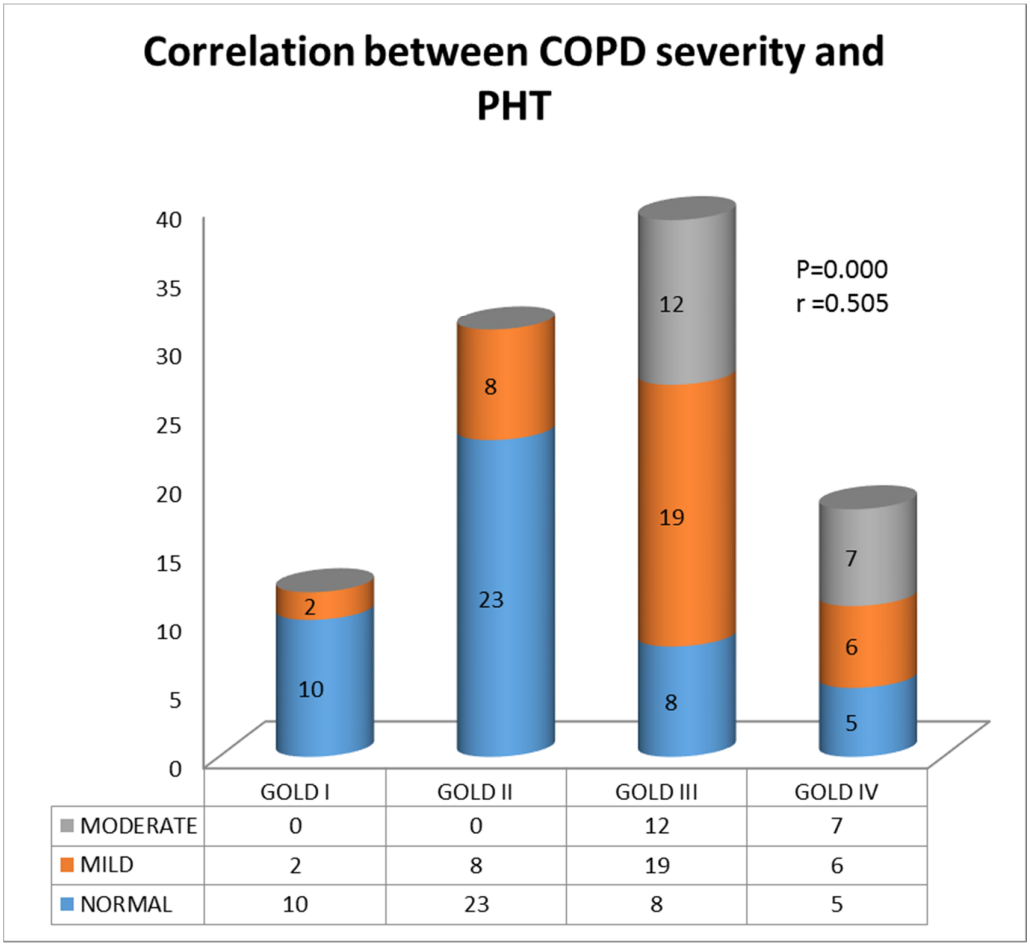


Fig.27 : Correlation between COPD severity and PHT

8.COPD-GRADE AND TAPSE

All the patients in the study population had TAPSE in the normal mean range indicating no RV systolic dysfunction The Mean TAPSE of GOLD I, GOLD II, GOLD III, GOLD IV COPD grades were 24,36,25,28mm respectively.

Table : 8 COPD Grade and TAPSE

GOLD GRADES	MEAN OF TAPSE (mm)
GOLD I	24
GOLD II	36
GOLD III	25
GOLD IV	28

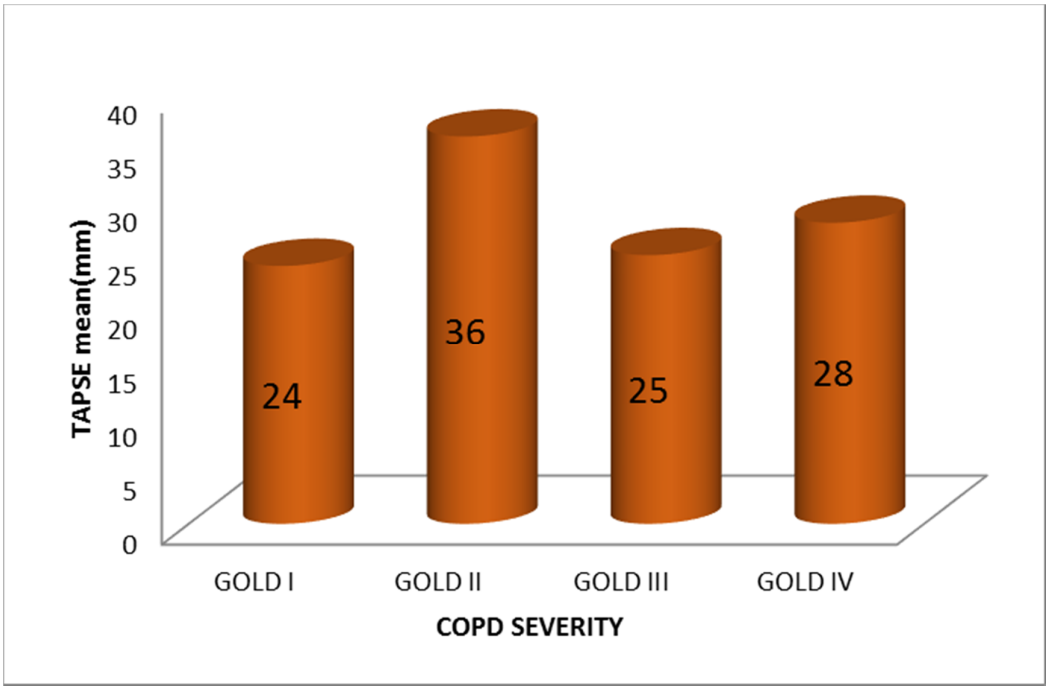


Fig.28 : COPD severity and TAPSE

9.COPD-GOLD GRADE AND TEI INDEX

In the 100 study subjects, 41(41%) had normal Tei index and 59(59%) had abnormal Tei index i.e. out of the normal mean range of Tei index. The number of people with abnormal TEI index in mild, moderate, severe and very severe COPD were 3(25%),12(38.70%),30(76.92%) and 14(77.77%) respectively.

Table 9 : COPD Gold Grade and TEI Index

GOLD-COPD STAGING	TEI INDEX		
	NORMAL	ABNORMAL	TOTAL
I	9	3	12
II	19	12	31
III	9	30	39
IV	4	14	18
TOTAL	41	59	100

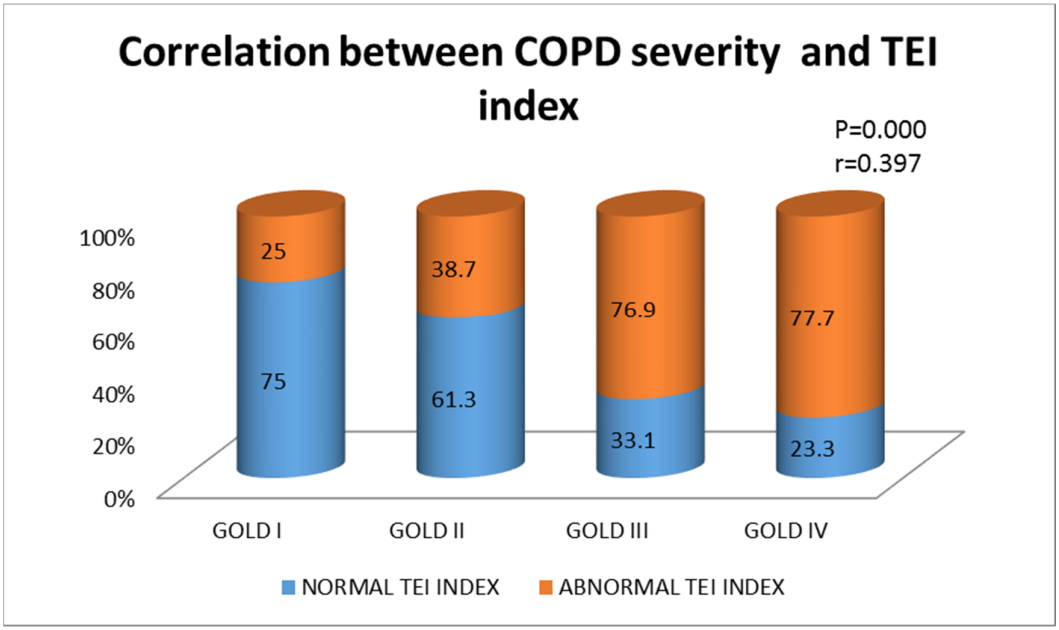


Fig. 29 : COPD severity and Tei index

10.PHT AND TEI INDEX

Among the 48 patients with normal PHT, 8 (17.39%) had abnormal Tei index, whereas of the 35 patients with mild PHT, 32 (91.42%) had abnormal Tei index and all the 19 (100%) patients with moderate PHT had abnormal Tei index.

Table 10 : Severity of PHT

SEVERITY OF PHT	TEI INDEX		
	NORMAL	ABNORMAL	TOTAL
NORMAL	38	8	46
MILD	3	32	35
MODERATE	0	19	19
TOTAL	41	59	100

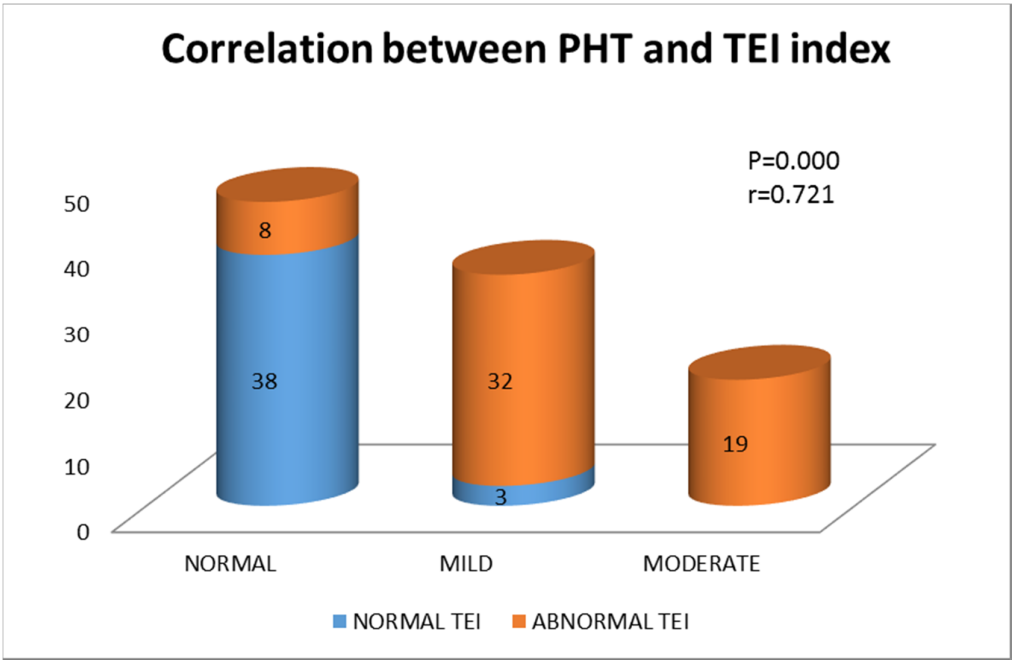


Fig.30 : PHT and Tei index

11.COPD AND EF

Out of the 100 COPD patients 5% had ejection fraction below 55% indicating LV systolic dysfunction.95% had normal ejection fraction. The mean ejection fraction of the study population was 63.75%.

Table 11 : COPD and Ejection Fraction

EJECTION FRACTION	NO.OF.PATIENTS
NORMAL	95
ABNORMAL	5
TOTAL	100

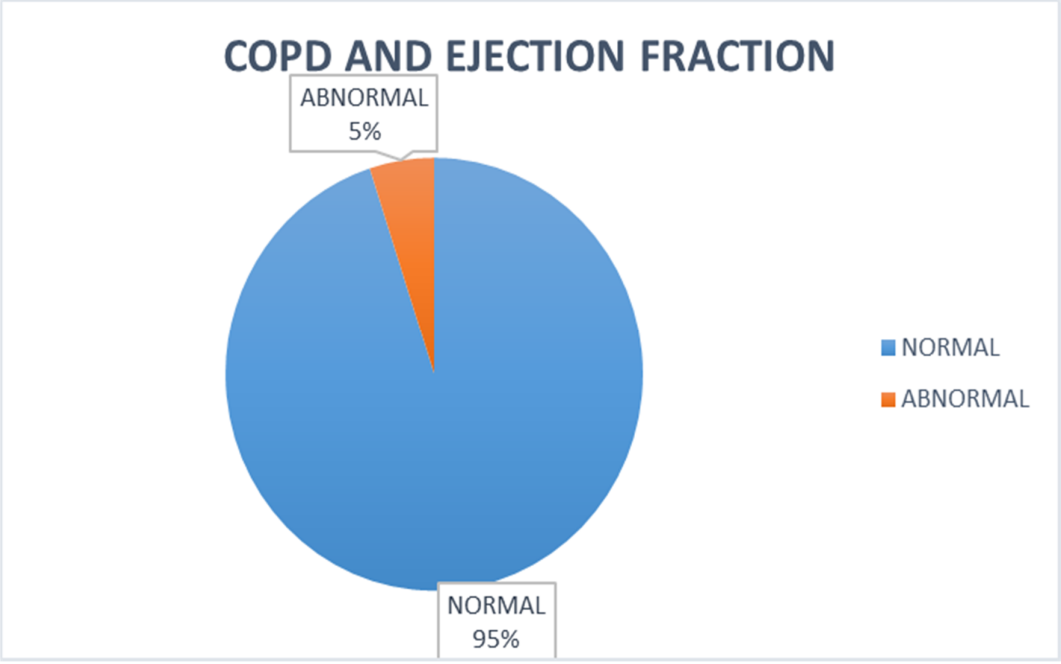


Fig.31 : COPD and Ejection fraction

12.COPD-GOLD GRADE AND EJECTION FRACTION

The mean Ejection fraction of mild, moderate, severe, and very severe COPD were 69.58, 63.90, 62.78, and 61.72 respectively.

Table :12. Gold COPD Staging and Ejection Fraction

GOLD-COPD STAGING	EJECTION FRACTION (%)		
	MAXIMUM	MINIMUM	MEAN
I	73	60	69.58
II	71	56	63.90
III	74	25	62.76
IV	72	36	61.72

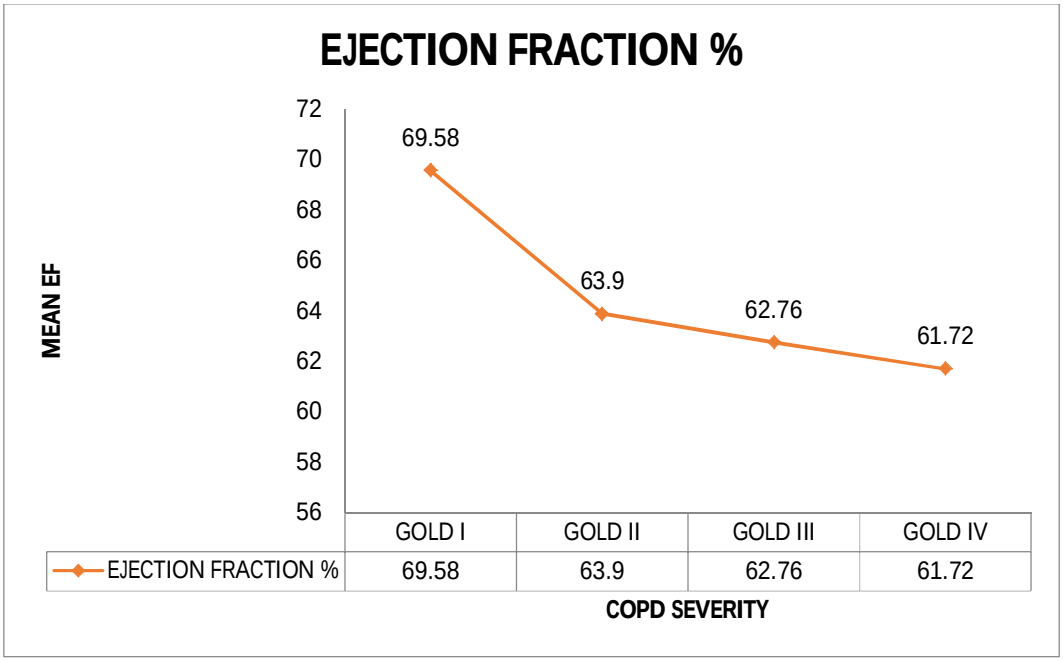


Fig.32 : COPD severity and ejection fraction

13.COPD-GOLD GRADE AND LVDD

Of the 100 COPD study subjects, 73(73%) had no LV dysfunction and 27(27%) had LV dysfunction. Out of the 27 patients with LV dysfunction, 21(77.77%) had grade I LV Diastolic dysfunction, 4(14.81%) had grade II LVDD and 2(7%) had grade III LVDD. The number of patients with LVDD in mild, moderate, severe and very severe COPD were 2/12(16.66%), 6/31(19.35%), 10/39(33.33%) and 9/18 (50%) respectively.

Table 13 : LV DIASTOLIC DYSFUNCTION

GOLD GRADE	LV DIASTOLIC DYSFUNCTION				TOTAL
	D0	D1	D2	D3	
I	10	2	0	0	12
II	25	6	0	0	31
III	29	7	1	2	39
IV	9	6	3	0	18
TOTAL	73	21	4	2	100

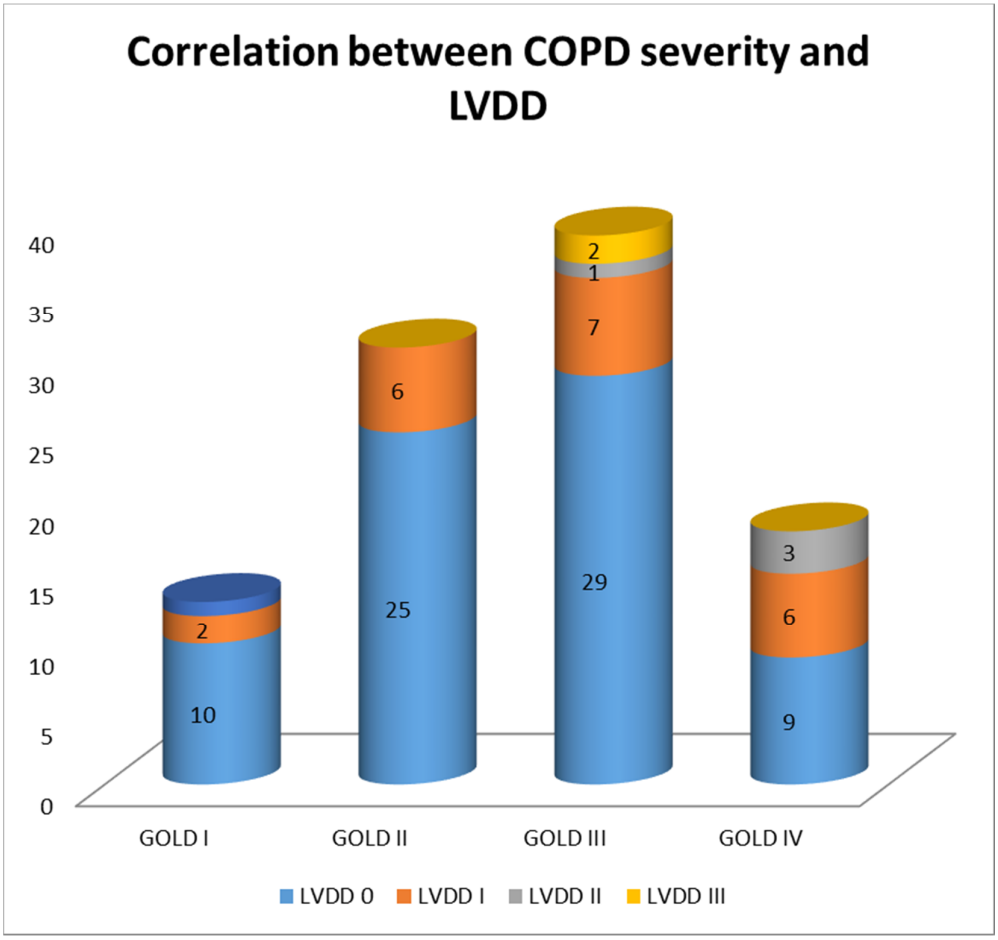


Fig. 33 : Correlation between COPD severity and LVDD

14.PHT AND LVDD

The number of patients with LVDD in patients with mild and moderate PHT were, 11/35(31.42%) and 8/19 (42.10%) respectively

Table 14 : PHT & LVDD

SEVERITY OF PHT	GRADING OF LVDD					
	D0	D1	D2	D3	D4	TOTAL
NORMAL	39	5	1	1	0	46
MILD	24	11	0	0	0	35
MODERATE	10	5	3	0	1	19
TOTAL	73	21	4	1	1	100

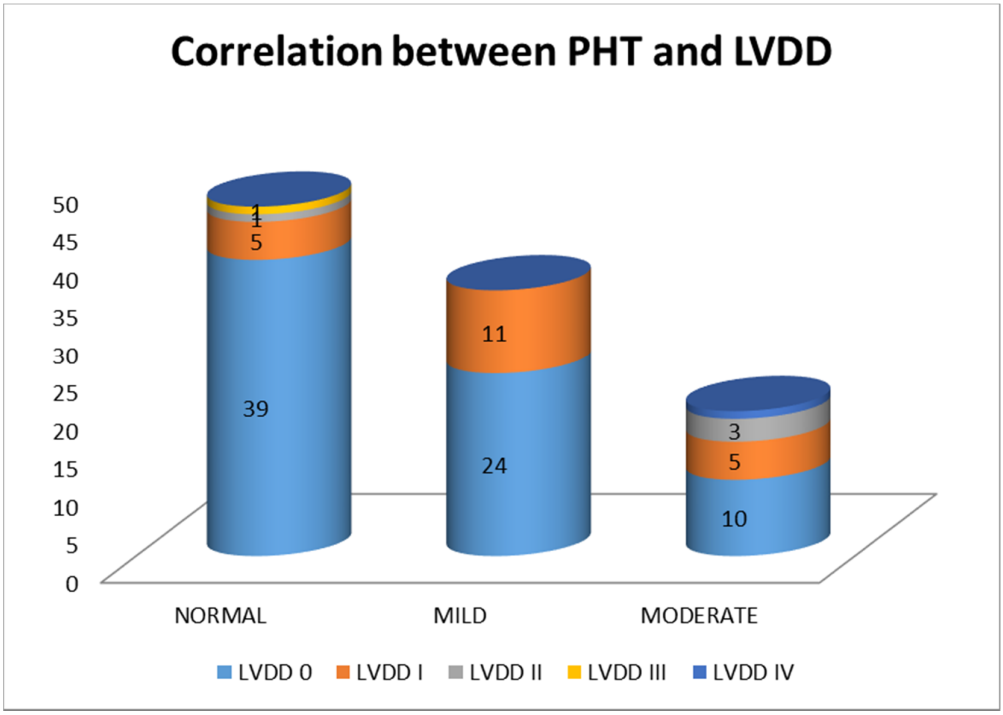


Fig. 34 : Correlation between PHT & LVDD

Discussion

DISCUSSION

PATIENT CHARACTERISTICS

1) AGE DISTRIBUTION

1. Age group of our study population ranged from 42 to 86 years.
2. The mean age of the study population was 59.31 with the standard deviation of 9.230 (59.31±9.230).
3. The number of patients in the age group of 40-50,51-60,61-70,71-80,and >80 years were 21,32,42 ,3 and 2 respectively.
4. Most of the patients in our study belonged to 50 – 70 years (74%)
5. Mean age of our study population was 59.31±9.23

Comparison between our study and other studies

STUDY	MEAN AGE OF STUDY POPULATION
Our study	**59.31 ± 9.23**
George Christian et al	**59.1 ± 1.7**
Rabab et al	**55.1 ± 7.3**

1. Mean age of male and female of our study population was similar to that in study by N.K.jain et al.

STUDIES	MALE	FEMALE
Our study	59.77+/- 9.41	55.54 +/- 6.8
N.K. Jain et al	61.57+/- ±10.37	58.34+/- 9.99

Most females with COPD were younger than males indicating that females develop COPD early than males. This finding correlated with the study by N.K.Jain et al

This could be attributable to the biomass smoke exposure which begins early in females who start cooking using wood stoves at a very early age and also, sleep and eat in the same room where they cook.

2) GENDER DISTRIBUTION

1. In our study, out of 100 patients, 89 were males and 11 were females. Thus males accounted for 89% of our study population while females accounted for 11%.
2. In the past, most studies showed that COPD prevalence was high among men than women. This is reflected in our study also.
3. Due to the increase in smoking habit in females, now studies report increasing prevalence of COPD among females.
4. When compared to the gender distribution in the study by N.K.Jain et al, the percent of females in our study was less. Because they enrolled more females to study the difference in COPD character in relation to gender.

Comparison between our study and other different studies

STUDY	MALE (%)	FEMALE (%)
Our study	**89**	**11**
Rabab et al	**83.3**	**16.7**
Lopez et al	**87.5**	**12.5**

3) SMOKING INDEX AND COPD GRADE

1. Majority of our study subjects were moderate smokers (47%).
2. Among GOLD I COPD patients, majority were light smokers (66.6%),
3. Among GOLD II and III COPD, majority were moderate smokers (64.52%) and (53.85%)

1. Among GOLD IV COPD, majority were heavy smokers (61.11%).
2. Thus, as smoking severity was increased, COPD severity also increased.
3. Females in our study had the mean FEV1 of 35.72%
4. Among Males, light smokers had mean FEV1 of 69.5%, moderate smokers had meanFEV1 of 50.46%, and heavy smokers had mean FEV1 of 33.33%.It clearly indicated that as smoking increased FEV1 decreased. There was a strong negative correlation in our study between FEV1 and Smoking Index (r -0.406).
5. Cigarette smokers had a high annual rate of decline in FEV1 of about 50 -60 mL, which was nearly double the average value of 30mL annually present in non-smokers. (Crofton 629)

4) SEVERITY OF COPD

1. In our study majority of men were having moderate and severe COPD. Whereas females had severe and very severe COPD.
2. Women were more susceptible to lung injury from smoking than men as they showed more lung function reduction in association with lower total exposure and they predominate among individuals with early onset of COPD and never-smokers with COPD.[16]
3. In GOLD I COPD, 83% of patients were in the 40-50years age group.
4. In GOLD II COPD,45% were in the51-60years age group
5. In GOLD III COPD,48.75% were in the 61-70 years age group
6. In GOLD IV COPD, 44.44% were in 61-70years age group.
7. Thus, with advancing age, severity of COPD is increased.
8. There was a significant correlation between severity of copd and age of the patients($p = 0.000$)

5) COPD AND PULMONARY HYPERTENSION

1. In our study, Out of the 100 patients, 54(54%) had Pulmonary hypertension.
2. Vadim Fayngersh et al study named " Pulmonary Hypertension in a Stable Community-Based COPD Population" in which they found that in 105 individuals with demonstrable TR jet, 63(60%) had PH
3. Rabab et al, in their study "LV function in patients with or without PH" comprising 36 COPD and 12 matched control group, reported 55.6% prevalence of pulmonary hypertension.
4. N.K.Gupta et al reported a prevalence of 63% pulmonary hypertension.
5. Scharf et al reported a very high incidence of 91% PH whereas weitzenblum reported 35% PH in their study.
6. This variable prevalence of PH in different studies has been attributed to the different cut-off value for PH and difference in the population characteristics of study subjects.
7. In our study, as the severity of COPD increased, the frequency of PH also increased, from 25% in GOLD I COPD to 72.22% in GOLD IV COPD.
8. No one in our study had severe pulmonary hypertension.
9. In the article "Pulmonary hypertension in chronic obstructive pulmonary disease" by Barbera et al concluded that Severe PH (defined as mPAP > 40 mm Hg) was uncommon (1–3%) in COPD.

10. In the study “Severe pulmonary hypertension and chronic obstructive pulmonary disease” with 998 COPD patients (median FEV1 = 50% of predicted), Chaouat et al reported that the prevalence of severe PH (PPA > 40 mm Hg) was 2.7%. But 50% of them had non-COPD etiologies to explain that. Thus the prevalence of severe PH is uncommon in COPD.

Frequency of PH in various studies

STUDY	FREQUENCY OF PH (%)
Our study	54
Vadim et al	60
Rabab et al	55.6
N.K.Gupta et al	63
Scharf et al	91
Weitzenblum et al	35

6) COPD AND TAPSE

1. TAPSE value of all our patients was above 16mm indicating no RV systolic dysfunction in our study.
2. In patients with COPD, because of the mild elevations in afterload and the slow disease progression, the right ventricle has a chance to adapt with hypertrophy, and RV systolic failure may not occur in the absence of comorbidities when patients are in a long-term stable state.
3. Most patients with COPD-associated PH had preserved RV contractility if studied during periods of clinical stability,[38] and studies had demonstrated RV systolic failure only among patients in the acutely decompensated state.[38]
4. Since all our patients were clinically stable COPD patients, they had preserved RV systolic function.

7) COPD AND TEI INDEX

5. In the 100 study subjects, 41(41%) had normal Tei index and 59(59%) had abnormal Tei index.
6. The number of people with abnormal TEI index in mild, moderate, severe and very severe COPD were 3(25%), 12(38.70%), 30(76.92%) and 14(77.77%) respectively.
7. Thus the Prevalence of abnormal Tei index had a linear relationship with severity of COPD
8. In our study there was a statistically significant correlation between Tei index and severity of COPD.
9. In the 35 patients with mild PHT, 32 (91.42%) had abnormal Tei index and all the 19 (100%) patients with moderate PHT had abnormal Tei index.
10. There was a significant correlation between Tei index and pulmonary hypertension in our study (P value 0.000) and also there was a strong positive correlation between them($r = 0.721$).
11. If the severity of pulmonary hypertension increased, there occurred an increase in the Tei index value suggesting RV global function impairment...

8) COPD AND LV FUNCTION

1. In our study, out of the 100 COPD patients, 5% had ejection fraction below 55% indicating LV systolic dysfunction.95% had normal ejection fraction. The mean ejection fraction of the study population was 63.75%.
2. It was an incidental finding (IHD) found out during the echocardiographic examination of the study subjects.
3. Unless there was an inherent IHD, LV systolic function was usually preserved in COPD Patients.
4. Prevalence rates of left ventricular systolic dysfunction in patients with COPD ranged from 4 to 32% and are usually associated with concomitant coronary heart disease.20–23.the prevalence of LV systolic dysfunction was 5% in our study and all were due to coronary artery disease.
5. Martha Lopez et al reported a high prevalence (90%) of LV diastolic dysfunction in stable severe COPD
6. In our study, the prevalence of LV diastolic dysfunction in severe and very severe stable COPD was lower (33.33%)
7. Past Studies indicated that the prevalence of mild LVDD in people older than 65 years with a normal LVEF is 21.7% and this increased to 27% in those older than 70 [17,18].

8. In the study by Martha Lopez et al, mean age of study population was 65+/- 7, whereas in our study the mean age is 59.31+/-9.23.many of the patients were older and all of them were heavy smokers and continued smoking till the study had been undertaken.
9. Because of these reasons the incidence of LVDD was high in that study.
10. Similar to the study by Lopez et al, there was no correlation between SPAP and degree of LVDD in our study.

Summary

SUMMARY

In our study with 100 stable COPD patients, we found that

1. Prevalence of COPD in female was lower than males.
2. When compared to males, female were somewhat younger in age because females develop COPD early due to their increased susceptibility to lung injury by smoke exposure.
3. There was a strong negative correlation between smoking index and FEV1%
4. Frequency of pulmonary hypertension increased linearly with the severity of COPD
5. There was a significant correlation between severity of COPD and pulmonary hypertension in our study.
6. Severe pulmonary hypertension was uncommon in stable COPD patients.
7. Stable COPD patients with pulmonary hypertension had preserved RV contractility (TAPSE) when they were in stable state for a long time and in the absence of other comorbidities.
8. COPD patients had abnormal Tei index.
9. There was statistically significant correlation between Tei index and severity of COPD

11. There was a strong positive correlation between Tei index and pulmonary hypertension.
12. As the systolic pulmonary artery pressure was increased, Tei index value increased above the normal.
13. Unless there was a coexisting ischaemic heart disease, COPD patients had normal LV systolic function
14. There was no correlation with degree of LV dysfunction and SPAP.

Conclusion

CONCLUSION

1. Among the extra-pulmonary systemic co-morbidities, cardiac manifestations are one of the most common comorbidities.
2. Since there is an anatomical and functional relation between lungs and heart, any dysfunction that impacts any one of the organs will have consequences in the other organ.
3. So, all COPD patients have to be evaluated for the presence of cardiac abnormalities.
4. Similarly, all patients with cardiovascular diseases should be evaluated for the presence of concomitant airflow obstruction.
5. Even though COPD is a progressive disease with high mortality rate, early diagnosis of coexisting cardiac abnormalities will reduce the morbidity and mortality in COPD patients.

Limitations

LIMITATIONS

1. Sample size is small. Needs a study with large number of subjects
2. No control groups are included in this study
3. Smoking is a risk factor for both the cardiovascular diseases and COPD. Hence studies with “smokers without COPD” as matched control will bring out the real magnitude of cardiac abnormalities that would be contributed by COPD itself.

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Annexures

ABBREVIATIONS

COPD	-	Chronic obstructive pulmonary disease
mMRC	-	Modified Medical Research Council
FEV1	-	Forced expiratory volume in 1 second
TAPSE	-	Tricuspid Annular Plane Systolic Excursion
LVDD	-	Left Ventricular diastolic dysfuction
MPI	-	Myocardial Performance Index
EF	-	Ejection Fraction
CVD	-	Cardiovascular disease
CAHD	-	Coronary Artery Heart Disease
CAT	-	COPD Assessment Test
S.D	-	Standard deviation
ATS	-	American Thoracic Society
GOLD	-	Global initiaitive for obstructive lung diseases
PH/PHT	-	Pulmonary Hypertension
SPAP	-	Systolic Pulmonary Artery Pressure
PAP	-	Pulmonary Artery Pressure
mPpa	-	Mean Pulmonary Artery Pressure
LV	-	Left Ventricle

PROFORMA

Demographic data

Name : Address :

Age/ Sex :

Height,Weight, BMI: Mobile no:

Socio-economic status : Landline no:

Marital status: Married/Unmarried

CLINICAL DATA

Symptoms with duration :

a.Cough with expectoration;

b.fever;

c.breathlessness on exertion

d.Hemoptysis;

e.chest pain

f. LOA/LOW

.others

Co-morbid illness :

1.DM/HT/Heart diseases/Epilepsy/Others

Alcohol: Yes/No Duration:

Smoking:Yes/No Duration:

O/E:

VITALS

Spo2 :

PR :

RR :

BP :

INVESTIGATIONS :

XRAY CHEST

SPUTUM AFB SMEAR

HEMOGRAM

PFT

ECG

ECHO

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MASTER CHART

S. No	NAME	AGE	SEX	S.I	FEV1 %	GOLD	SPAP mmHg	PHT	TAPSE mm	TEI	LV DD	EF%
1	DEVARAJ	64	M	480	53	O	22.8	N	22.4	0.22	D0	67
2	DEVAN	65	M	180	55	O	21.2	N	22.8	0.22	D0	59
3	THANTHONI	54	M	280	34	S	19	N	16.9	0.23	D3	43
4	LATHA	45	F		44	S	19	N	23.9	0.23	D0	71
5	JAGADEESAN	47	M	120	82	M	19	N	20.4	0.24	D0	71
6	RAGHURAM	75	M	280	53	O	25	N	22.9	0.24	D0	59
7	VINCENT	54	M	140	54	O	19.9	N	23	0.24	D0	68
8	SHANMUGAM	63	M	240	55	O	24	N	23.4	0.24	D0	66
9	RAJENDRAN	63	M	80	65	O	18.9	N	19.4	0.25	D0	61
10	MURUGAN	48	M	90	90	M	20.2	N	20.3	0.25	D0	72
11	SELVAM	48	M	110	93	M	22.4	N	22.8	0.25	D0	71
12	EKAMBARAN	56	M	80	54	O	19.6	N	23.5	0.25	D0	67
13	NEEDHI	42	M	100	46	S	19.5	N	17	0.26	D0	74
14	PADMA	50	F		34	S	22	N	24.2	0.26	D0	70
15	VENKATESAN	45	M	48	81	M	19.9	N	17.1	0.27	D0	72
16	MOHAN	42	M	60	82	M	24	N	24	0.27	D0	72
17	DILLIKUMAR	56	M	280	57	O	24	N	24.2	0.27	D0	68
18	JOE	64	M	80	61	O	25	N	20.7	0.28	D0	65
19	NATARAJ	63	M	80	67	O	24.9	N	22	0.28	D0	66
20	SABARINATHAN	45	M	72	86	M	22	N	23	0.28	D0	70
21	SUMATHI	50	F		47	S	23	N	23.4	0.28	D0	72
22	JAYAPAL	56	M	420	54	O	19	N	23.9	0.28	D0	66
23	CHANDRAN	58	M	300	55	O	23	N	20.2	0.29	D0	68
24	CHELLAPPA	56	M	300	55	O	25	N	23.7	0.29	D0	68
25	GOVINDASAMY	60	M	150	56	O	20.7	N	19.6	0.3	D0	63
26	MANOHAR	50	M	80	87	M	23.1	N	21.5	0.3	D1	68
27	CHANDRAN	65	M	260	52	O	23	N	24.3	0.3	D0	59
28	DEVADOSS	49	M	150	80	M	23.1	N	20.3	0.31	D0	68
29	PANNEERSELVAM	60	M	80	25	V	19.9	N	21.7	0.31	D0	66
30	KALIVARATHAN	42	M	75	81	M	22	N	22.3	0.31	D0	73
31	BABU	67	M	200	29	v	20.3	N	23.8	0.31	D0	61
32	KUMAR	45	M	90	79	O	20	N	24	0.31	D0	71
33	DURAISAMY	61	M	130	54	O	18	N	19.4	0.32	D0	66
34	KARUPPAN	51	M	300	54	O	22	N	22.8	0.32	D0	65
35	BALASUNDARAM	48	M	400	49	S	18.7	N	23.6	0.32	D0	72
36	RAVEENDRAN	56	M	380	31	S	25	N	17	0.33	D2	64
37	EBINESAR	51	M	380	28	V	23	N	22.6	0.34	D0	65
38	BALAN	65	M	300	29	V	23	N	17.5	0.35	D1	66
39	THIRUVENGADAM	70	M	360	36	S	35.9	MILD	18.9	0.35	D0	59
40	MANICKAM	65	M	180	39	S	37.2	MILD	19.9	0.35	D0	63
41	MANI.R.K	64	M	520	28	V	35.8	MILD	23.1	0.35	D1	65
42	CHINNAPPAN	70	M	490	24	V	35.4	MILD	16.5	0.36	D0	56
43	NITHYANANDHAM	53	M	200	72	O	35.5	MILD	17	0.36	D0	65
44	VENUGOPAL	65	M	450	25	V	36.2	MILD	17	0.36	D1	61
45	RANI	55	F		46	S	37.9	MILD	17.2	0.36	D0	68
46	RANGASAMY	60	M	700	52	O	36.9	MILD	18	0.36	D0	60
47	RAMALINGAM	70	M	120	40	S	36.2	MILD	18	0.36	D1	69
48	MOINUDEEN SHERIF	45	M	500	25	V	36.1	MILD	18.2	0.36	D0	72
49	RAVI	50	M	78	81	M	20.9	N	19.9	0.36	D0	70
50	NARENDHERAN	65	M	280	48	S	35.8	MILD	19.9	0.36	D0	62

S. No	NAME	AGE	SEX	S.I	FEV1 %	GOLD	SPAP mmHg	PHT	TAPSE mm	TEI	LV DD	EF%
51	PERUMAL	68	M	150	46	S	36	MILD	20.9	0.36	D0	59
52	RAJENDRAN	54	M	70	67	O	37.9	MILD	21.2	0.36	D1	56
53	KARIKALAN	52	M	270	58	O	19	N	21.9	0.36	D0	66
54	CHELLAIYA	68	M	300	44	S	36.1	MILD	22.8	0.36	D0	59
55	NATRAJ	45	M	280	54	O	36.2	MILD	16.9	0.37	D1	70
56	HARIKRISHNAN	61	M	320	34	S	38.2	MILD	17	0.37	D0	65
57	GOVINDASAMY	70	M	280	45	S	36.1	MILD	17	0.37	D1	71
58	SUBRAMANI	57	M	320	18	V	35.9	MILD	17	0.37	D0	63
59	MOHAN	55	M	260	32	S	37.2	MILD	17.8	0.37	D0	63
60	MATHI MOSES	58	M	150	43	S	39.4	MILD	18	0.37	D1	61
61	SHANMUGAM	67	M	90	54	O	23.4	N	22.4	0.37	D0	69
62	POONGAVANAN	50	F		21	V	19	N	23.8	0.37	D0	65
63	RAMADOSS	66	M	280	55	O	18.9	N	24.3	0.37	D0	58
64	SAMINATHAN	70	M	150	51	O	19	N	18.4	0.38	D1	56
65	PADMANABAN	55	M	180	46	S	36.4	MILD	18.4	0.38	D0	67
66	NAINIAPPAN	65	M	300	32	S	36.1	MILD	18.9	0.38	D0	62
67	KONDALRAO	66	M	80	55	O	37.3	MILD	19.2	0.38	D1	56
68	HEMA	51	F		45	S	38.4	MILD	19.4	0.38	D0	65
69	NARAYANAN	70	M	300	64	o	35.8	MILD	22.1	0.38	D0	59
70	RAJAN	60	M	270	51	O	38.5	MILD	24.7	0.38	D0	65
71	NANDEESWARAN	53	M	300	39	S	37.4	MILD	18.3	0.39	D0	66
72	CHANDRA	60	F		29	V	36.1	MILD	24.3	0.39	D0	66
73	KALIDASS	68	M	280	59	O	22.8	N	20.3	0.4	D1	65
74	MURUGAN	70	M	60	91	M	35.1	MILD	19.1	0.41	D1	60
75	GAJENDRAN	78	M	280	33	S	35	MILD	19.8	0.41	D0	70
76	MARIAPPAN	55	M	105	83	M	36.1	MILD	19.6	0.44	D0	68
77	BALU	48	M	300	45	S	36.4	MILD	19.2	0.45	D1	50
78	AADHIMOOLAM	67	M	520	25	V	45.9	MOD	21.4	0.45	D2	48
79	SUSEELA	65	F		45	S	46.3	MOD	16.2	0.46	D0	66
80	KANTHA	60	F		36	S	46	MOD	16.4	0.46	D0	66
81	SAMY	69	M	400	33	S	46.2	MOD	17.9	0.46	D0	60
82	MANI.E	68	M	400	37	S	47	MOD	18.9	0.46	D0	59
83	JOSEPH STALIN	69	M	240	43	S	45.1	MOD	18.9	0.46	D0	60
84	ELUMALAI	85	M	280	43	S	46.2	MOD	19.8	0.46	D0	59
85	PALANI	65	M	600	30	S	45.1	MOD	20.8	0.46	D0	60
86	IRUSAPPAN	62	M	320	32	S	46.4	MOD	24	0.46	D0	66
87	VIJAYA	65	F		24	V	47.2	MOD	16.3	0.47	D1	65
88	NANDAGOPAL	50	M	460	29	V	46.1	MOD	17.9	0.47	D2	36
89	FAZOOL RAHMAN	54	M	370	29	V	46	MOD	18	0.47	D1	62
90	SAM	64	M	120	45	S	36.2	MILD	19	0.47	D0	68
91	DHARMARAJ	62	M	300	47	S	47.3	MOD	19.9	0.47	D1	61
92	THILAGA	60	F		22	V	46	MOD	19.9	0.47	D2	67
93	SAMMANDHAN	61	M	450	29	V	46.2	MOD	20	0.47	D0	69
94	ANTONY	52	M	400	38	S	47.3	MOD	20.3	0.47	D0	65
95	RAJAVELU	86	M	200	35	S	45	MOD	17	0.48	D1	61
96	SEKAR	55	M	270	56	O	37.4	MILD	18.1	0.48	D1	64
97	DEENAN	65	M	170	43	S	47.3	MOD	18.9	0.48	D4	25
98	HARI	61	M	300	34	S	38.4	MILD	19.2	0.48	D0	69
99	JAKKARIYA	77	M	340	29	V	45	MOD	24.3	0.48	D1	58
100	JOHNN BASHA	58	M	420	32	S	19	N	17.1	0.565	D1	58

KEYS TO MASTER CHART

S.I - SMOKING INDEX

TAPSE - TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSION

SPAP - SYSTOLIC PULMONARY ARTERIAL PRESSURE

LVDD - LEFT VENTRICULAR DIASTOLIC DYSFUNCTION

PHT - PULMONARY HYPERTENSION

GOLD - GLOBAL INITIATIVE FOR OBSTRUCTIVE LUNG DISEASES

EF - EJECTION FRACTION

FEV1 - FORCED EXPIRATORY VOLUME IN 1 SECOND

PATIENT CONSENT FORM

STUDY DETAIL :

STUDY CENTRE :

PATIENT'S NAME :

PATIENT'S AGE :

IDENTIFICATION NUMBER :

I confirm that I have understood the purpose and procedure of the above study. I have the opportunity to ask questions and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that the sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However I understand that my identity would not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including haematological, biochemical, radiological tests.

Signature/thumb impression:

Patient's name and address:

Place: Date:

Signature of the investigator:

Name of the investigator:

Place: Date:

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1. ÷©ØSÔ¨¤mkÒÍBµõ´a]°ß÷{õUPzøu²®£¯øÚ²®¬ÊÁx©õP ¦¶¢xöPõs÷hß.÷©¾®GÚxAøÚzx\¢÷uP[PøÍ²® ÷PmkAuØPõÚÂÍUP[PøÍ²®öuÎÄ£kzvUöPõs÷hß.
2. ÷©¾®C¢uBµõ´a]USGÚxö\õ¢uÂ¸¨£zvß÷£¶À£[÷PØQ÷ÓßGßÖ®, ÷©¾®G¢u÷{µzv¾®GÆÂu¬ßÚÔÂ¨¦ªßÔC¢uBµõ´a]°¼¸¢xÂ»P ¬Êø©¯õÚE¶ø©EÒÍøu²®, CuØSGÆÂu\mh¤øn¨¦®CÀø» Gß£øu²®AÔ÷Áß.
3. Bµõ´a]¯õÍ÷µõ, Bµõ´a]EuÂ¯õÍ÷µõ, Bµõ´a]E£¯zuõ÷µõ, Bµõ´a] ÷£µõ]¶¯÷µõ, KÊ[Sö{Ô ö\¯ØSÊEÖ¨¤ÚºP÷ÍõG¨÷£õx÷Ás k©õÚõ¾® GÚxAÝ©v°ßÔGÚxEÒ÷{õ¯õ Î £vÄPøÍC¢uBµõ´a]UPõP÷ÁõAÀ»xGvºPõ»¤Ó Bµõ´a]PÐUPõP÷Áõ £¯ß£kzvUöPõÒÍ»õ®GßÖ®÷©¾®C¢u|£¢uøÚ{õßCÆÁµõ´a]°¼¸¢x Â»QÚõ¾®uS®GßÖ®J¨¦UöPõÒQ÷Óß.B°Ý®GÚxAøh¯õÍ® \®£¢u¨£mhG¢u£vÄPÐ®(\mh§ºÁ©õÚ÷uøÁPÒuÂµ) öÁÎ°h¨£h©õmhxGßÓEÖvö©õÈ°ß ö£¯¶À C¢uBµõ´a]°¼¸¢x QøhUP¨ö£Ö®¬iÄPøÍöÁÎ°h©Ö¨¦ öuÔÂUP©õm÷hßGßÖEÖv¯ÎUQß÷Óß.
4. C¢uBµõ´a]US{õß¬Ê©Úxhß\®©vUQß÷ÓßGßÖ®÷©¾®Bµõ´a]U SÊÂÚºGÚUSAÎUS®AÔÄøµPøÍuÁÓõx¤ß£ØÖ÷ÁßGßÖ® EÖv¯ÎUQß÷Óß.
5. C¢uBµõ´a]USz÷uøÁ¨£k®AøÚzx©¸zxÁ¨£¶÷\õuøÚPÐUS® Jzxøç¨¦u¸÷ÁßGßÖEÖv¯ÎUQß÷Óß.
6. C¢uBµõ´a]US¯õ¸øh¯ÁØ¦Özu¾ªßÔGÚxö\õ¢uÂ¸¨£zvß÷£¶¾® _¯AÔÄhÝ®¬Ê©ÚxhÝ®\ம்மத்திக்கின்றேன்என்றுஇதன் மூலம் J¨¦UöPõÒQ÷Óß.

÷{õ¯õ Î °ßøPö¯õ¨£®/ö£¸ÂµÀøP÷µøP:

Ch®: ÷uv:

Bµõ´a]¯õÍ¶ßøPö¯õ¨£®:

Ch®: ÷uv:

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10

Protocol ID. No.14/02/2015 Dt:27/02/2015

CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "To evaluate the presence of cardiovascular abnormalities andits association with the severity of airway obstruction in stable copd patients"- For Project Work submitted by Dr.M.Saravanan, Post Graduate in TB and Chest Diseases, Govt. Kilpauk Medical College, Chennai.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

GOVT. KILPAUK MEDICAL COLLEGE
27 MAR 2015

CHAIRMAN,
Ethical Committee
Govt. Kilpauk Medical College, Chennai